„Koronare Interventionen in der Therapie der multifokalen Atherosklerose“

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Verzeichnis **Seitenangabe**

1. Einführung

Die Atherosklerose ist die bedeutendste humane Gefäßkrankheit mit bevorzugtem Befall der großen und mittelgroßen Arterien vom muskulären und elastischen Typ (1, 2). Die ersten atherosklerotischen Läsionen sind bereits ab frühem Kindesalter nachweisbar (3), später werden die Läsionen komplexer (4) und ubiquitärer (5). Am deutlichsten ist in der Regel die Bauchaorta betroffen (6). Eine Reihe von Risikofaktoren der Atherosklerose wurde beschrieben (7); als Hauptrisikofaktoren gelten Störungen des Lipoproteinstoffwechsels, arterielle Hypertonie, Diabetes mellitus, Rauchen, genetische Vorbelastung und Alter (8); ihre Wichtung ist jeweils nach Gefäßregion unterschiedlich (9). Die molekulare Pathogenese der Atherosklerose wurde bisher nicht eindeutig geklärt (10). Als gemeinsames pathogenetisches Prinzip wird eine entzündliche Reaktion auf eine primäre Schädigung des Endothels im Sinne einer Verletzungsreaktion („*response-to-injury" hypothesis*) angesehen (11). Im Verlauf der Erkrankung kommt es zu einer zunehmenden Verdickung der Gefäßwände, welche anfänglich durch eine Gefügedilatation (*positive remodeling*) kompensiert werden kann (12). Nach Ausschöpfung der Kompensationsreserven (in der Regel dann, wenn die Plaquelast 40% der durch die Elastika interna umschriebenen Fläche überschreitet) kommt es zu einer Verengung des Gefäßlumens und konsekutiver Minderdurchblutung der Endorgane. Diese in der Regel langsam fortschreitende Verdickung der Arterienwände wird von akuten athero-thrombo-embolischen Komplikationen überlagert (13, 14). Klinisch wird die Atherosklerose durch Organischämien manifest.

Traditionell wurden die Gefäßkrankheiten chirurgisch und internistisch behandelt. Während in der Chirurgie die Gefäßkrankheiten ursächlich als solche behandelt wurden, beschränkten sich in den internistischen Fächern die Behandlungen auf die Folgeerkrankungen (Organischämien). Zum Beispiel wurde der Herzinfarkt bis in die frühen 1980-er Jahre konservativ-medikamentös behandelt (15). Patienten mit klinisch manifester Atherosklerose in unterschiedlichen Gefäßregionen wurden den jeweiligen für die betroffenen Organe zuständigen Fachdisziplinen zugeordnet.

Die Einführung der lokalen (16) und der systemischen (17) koronaren Fibrinolyse und dann insbesondere die Einführung der akuten Koronarinterventionen in der Therapie des akuten Herzinfarktes in den 1980-er Jahren (18) haben auch die internistischen Behandlungen auf die kausal betroffenen Gefäße ausgerichtet und das traditionelle Organkonzept in Frage

gestellt. Außerdem haben die Fortschritte in der Gefäßtherapie das Spektrum der Behandlungsoptionen erweitert und den Trend zu weiteren Subspezialisierungen innerhalb der etablierten Fachdisziplinen verstärkt; ein weiteres Auseinanderdriften der vaskulären Fachkompetenzen schien unvermeidlich. Patienten mit einer klinisch bedeutsamen multifokalen Atherosklerose sahen sich in der Regel mit einer größeren Anzahl von Spezialisten und Behandlungskonzepten konfrontiert.

Das panvaskuläre Konzept wurde Anfang 2000 mit dem Ziel entwickelt, die unterschiedlichen vaskulären Fachkompetenzen zu vernetzen und durch ihre Bündelung sinnvolle Synergien im Bezug auf die Versorgungsqualität und Verwendung von Ressourcen zu realisieren. Obwohl die Bündelung der komplementären Fachkompetenz allen Gefäßpatienten zugutekommt, sind besondere Vorteile bei Patienten mit komplexen, multifokalen und seltenen Krankheitsbildern zu erwarten. Insbesondere bei diesen Risikogruppen sind für den angestrebten Therapieerfolg optimale, innerhalb eines Kompetenzteams abgestimmte Behandlungsstrategien von besonderer Bedeutung (19). Das panvaskuläre Konzept wurde umfassend dokumentiert (Abbildung 1) (20), vielfach aufgegriffen und weiterentwickelt (Abbildung 2).

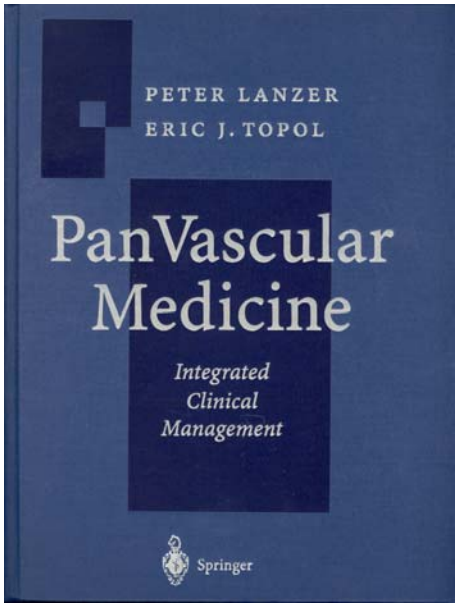

Abbildung 1. Titelseite des Lehrbuchs zum panvaskulären Behandlungskonzept, Springer Verlag, 2002 (20).

Abbildung 2. Panvaskuläres Konzept der Deutschen Gesellschaft für Gefäßchirurgie und Gefäßmedizin, Jahrestagung 2012.

1.1. Multifokale Atherosklerose

Der Systemcharakter der Atherosklerose wurde den Pathologen bereits im 19. Jahrhundert vertraut (21), seine Bedeutung wurde von den klinisch tätigen Ärzten allerdings erst in der zweiten Hälfte des 20. Jahrhunderts erkannt. Die ersten Hinweise auf die klinische Bedeutung der multifokalen Atherosklerose lieferten der Gefäßchirurg Norman Hertzer und der Herz- und Gefäßchirurg Michael DeBakey in den 1980-er Jahren. Hertzer und Mitarbeiter haben in ihrem Krankengut von 1000 Patienten mit Indikation zur operativen Versorgung einer peripheren arteriellen Verschlusserkrankung (PAVK) in 25% der Fälle koronarangiographisch eine schwere koronare Herzerkrankung, KHK, festgestellt. Eine schwere KHK wurde als mindestens eine Stenose größer als 70% des Durchmessers definiert (22). In einer weiteren Arbeit haben Hertzer und Mitarbeiter bei 506 Patienten mit einer zerebrovaskulären Erkrankung (symptomatische extrakranielle Karotis interna, Anzahl N=288; asymptomatisches Karotisstenosegeräusch, N=218 Patienten) in 37% der Fälle eine schwere KHK koronarangiographisch gesichert (23). DeBakey hat in einem Kollektiv von 13.827

Personen die Atherosklerose in fünf DeBakey Verteilungsmuster eingeteilt. Verteilungsmuster Typ V, bestehend aus der Kombination von ≥ 2 DeBakey-Verteilungsmustern I bis IV wurde bei 5.7% aller Patienten (mittleres Alter 60.8 Jahre, 73% Männer) festgestellt. Nach einer mittleren Beobachtungsdauer von 77.6 Monaten wiesen die Patienten mit dem DeBakey Verteilungsmuster V die häufigste systemische Progression der Atherosklerose (14.9%) auf (24). In der später in den 1990-er Jahren durchgeführten CAPRIE- Studie wurde die klinische Bedeutung der systemischen Ausbreitung der Atherosklerose bei Patienten mit ischämischen Organerkrankungen dokumentiert und die Bedeutung einer umfassenden Sekundärprävention belegt (25). In einer aktuellen Studie wurde das hohe kardiovaskuläre Risikopotential der Patienten mit multifokaler Atherosklerose (*polyvascular disease*) dokumentiert (26). Der Begriff der Gefäßmultimorbidität wurde als Vorhandensein einer klinisch manifesten Gefäßerkrankung in mindestens zwei voneinander unabhängigen Gefäßregionen definiert (19). In einer aktuellen Übersichtsarbeit wurden die klinischen Studien über die multifokale Atherosklerose zusammengestellt (27).

1.2. Koronare Katheter-vermittelte Revaskularisationsverfahren

Die Einführung der Katheter-vermittelten endovaskulären Verfahren hat den Paradigmenwechsel (primäre Behandlung des zuführenden Gefäßes statt des Endorgans) in der Therapie von Ischämiesyndromen ausgelöst. Diese Verfahren wurden in die Medizin am 16. Januar 1964 durch Charles Dotter und Melvin Judkins, beide Radiologen an der Oregon Health Sciences University in Portland, Oregon, eingeführt. An diesem Tag haben die beiden Ärzte bei einer 82- jährigen Patientin namens Laura Shaw eine hochgradig verengte linke Femoralarterie über einen nach Seldinger Methode gewonnenen arteriellen Zugang (28) mittels steifer Dilatatoren aus Teflon sukzessiv geweitet und erfolgreich revaskularisiert (29).

Zu den frühen Verfechtern dieser neuen perkutanen Methode der Gefäßtherapie gehörten in Deutschland insbesondere die Radiologen Werner Porstmann, Charite, Berlin, Eberhard Zeitler und Werner Schoop, beide Aggertal Klinik, Engelskirchen. Nach den experimentellen Arbeiten von Porstmann mit einem Korsett-Ballonkatheter (30) hat erst die Einführung des expandierbaren, doppellumigen und druckresistenten Ballonkatheters durch Andreas Grüntzig, Universität Zürich (31) der perkutanen Methode der Gefäßtherapie den Durchbruch

verschafft. Grüntzigs doppellumiger Ballonkatheter ermöglichte sowohl Gefäßdilatationen mittels des am distalen Ende des Katheters angebrachten Ballons als auch Druckmessungen bzw. Kontrastmittelgaben zur selektiven Gefäßdarstellung. Der Dilatationsballon aus Polyvinylchlorid, PVC, hatte einen Durchmesser von 3 bis 5mm und konnte mit Hochdruck, bis ca. 7 bar, aufgedehnt werden. Die ersten Dilatationskatheter dieser Art wurden kommerziell durch die Firma Schneider- Medintag, Zürich hergestellt. Der Ballonkatheter wurde in das Zielgefäß über einen 9French Führungskatheter eingeführt und mit einem am distalen Ballonende angebrachten kurzen Führungsdraht gesteuert. Die ersten klinischen Anwendungen der Ballondilatation führte Grüntzig nach tierexperimenteller Validierung (32) an peripheren Arterien und (33) und an Nierenarterien (34) durch.

Nach einer Modifizierung des doppellumigen Katheters für den Einsatz in den Koronargefäßen (35, 36) und nach tierexperimentellen Untersuchungen (37, 38) wurde die erste Katheter-vermittelte Ballondilatation eines Koronargefäßes am Menschen am 9. Mai 1977 im St. Mary's Hospital, San Francisco intraoperativ von Grüntzig vorgenommen (39). Am 16. September 1977 führte dann Grüntzig im Universitätsklinikum Zürich die erste perkutane koronare Dilatation in einem Katheterlabor in kardiochirurgischer Bereitschaft durch (40, 41). Der Patient Adolf Bachmann, ein 38-jähriger Versicherungskaufmann, hatte klinisch eine instabile Angina pectoris bei koronarangiographischem Nachweis einer proximalen Ramus interventricularis anterior Stenose.

Die ersten Dilatationskatheter waren im Koronarsystem aufgrund ihrer Steifigkeit und Robustheit nur schwer steuerbar, so dass meist nur proximale, konzentrische und nicht-verkalkte Stenosen in geraden Koronarsegmenten einer endovaskulären Behandlung zugänglich waren (42). Spätere Fortschritte in der Kathetertechnologie haben die mechanischen Eigenschaften und die manuelle Handhabung der koronaren Dilatationskatheter verbessert und dadurch ihre klinischen Einsatzmöglichkeiten erweitert. Zu den wesentlichen Verbesserungen in der Kathetertechnologie gehörten die Entwicklung eines frei beweglichen mit Teflon beschichteten 175 cm langen, koronaren Führungsdrahts mit einem 0.46 mm (0.018 Zoll) Durchmesser und einer als J-geformten flexiblen Spitze. Die koronare co-axiale Über-den-Draht-Technik (*co-axial over-the-wire technique, OTW*) wurde damit 1982 durch John Simpson eingeführt (43). Der frei bewegliche koronare Führungsdraht hat den Vorschub und die Steuerbarkeit der Dilatationskatheter deutlich verbessert. Die Einführung der 300cm langen koronaren Führungsdrähte (Austauschdrähte) mit der „langen Führungsdraht-Technik"

durch Martin Kaltenbach (44) hat es ermöglicht, bei einem Wechsel des Ballonkatheters den Führungsdraht im Koronargefäß zu belassen und dadurch während der gesamten Prozedur die Kontrolle über das koronare Zielgefäß zu behalten. Die lange Führungsdraht-Technik hat das Aktionsrisiko der koronaren Interventionen spürbar reduziert und eine deutlich schnellere Arbeitsweise ermöglicht. In Abwandlung der Kaltenbach- Methode wurden später Verlängerungsdrähte (*extension wires*), die an die Führungsdrähte mit normaler Länge angekoppelt werden konnten (*docking*), eingeführt. Einen wesentlichen Fortschritt für die koronaren Interventionen bedeutete die Einführung der durch eine Verkürzung des Lumens für den Führungsdraht modifizierten Ballonkatheter. Eine externe, zum Schaft des Katheters parallel verlaufende kurze Drahtführung hat Björn Nordenström bereits 1962 vorgeschlagen (45). Ein für die klinische Anwendung praktikables Verfahren wurde jedoch erst in der Mitte der 1980-er Jahre als „*monorail*" Technik durch Tassilo Bonzel (46) und „*rapid exchange, Rx*" Technik durch Paul Yock (47) eingeführt. Die neue Technik hat die Anwendung von Führungsdrähten mit normaler Länge (140 cm bis 180 cm) ermöglicht. Im Weiteren war die neue Methodik in der Handhabung und in der Schnelligkeit insbesondere beim Wechsel der Dilatationskatheter der gängigen OTW- Technik deutlich überlegen. Durch die Verkürzung des zweiten Lumens und durch die externe Drahtführung wurde allerdings die Festigkeit des Schaftes (*push*) des Dilatationskatheters (*hypotube*) reduziert. Um die Leistungsfähigkeit der neuen Ballonkatheter bei steigenden klinischen Anforderungen zu erhalten bzw. zu verbessern, musste die Gleitfähigkeit und Festigkeit der Materialien erhöht werden. Durch den raschen technologischen Fortschritt wurden für die koronaren Interventionen in Kürze hochwertige Ballonkatheter mit zunehmend niedrigen Profilen, hochdruckresistenten Dilatationsballons und schmaleren, mit Metall verstärktem Schaft verfügbar. Aufgrund des geänderten Designs musste jedoch bei der Anwendung dieser Dilatationskatheter auf die Möglichkeit einer distalen Kontrastmittelgabe und einer distalen intrakoronaren Druckmessung verzichtet werden. Ein weiterer Meilenstein in der koronaren Intervention bedeutete die Einführung der metallenen Gefäßstützen (*bare metal stents, BMS*) Ende der 1980-er Jahre (48, 49) sowie der um 2000 eingeführten, mit Polymeren beschichteten und mit Medikamenten, insbesondere mit Antimetaboliten, getränkten Gefäßstützen (*drug eluting stents, DES*) (50). Der Einsatz der modernsten Materialien und Herstellungstechnologien im Rahmen des industriellen Wettbewerbs hat den klinischen Einsatz einer hochwertigen Instrumentation bei koronaren Interventionen ermöglicht und sukzessiv den Einsatz dieser Produkte bei Interventionen in nichtkoronaren Gefäßen angeregt.

Neben der endoluminalen Angioplastie wurde in der Folgezeit eine Reihe von weiteren Verfahren der perkutanen koronaren Therapie wie die direktionelle Atherektomie (*directional atherectomy*) (51), Rotationsatherektomie (*rotablation*) (52), Excimer-Laserangioplastie (*excimer laser angioplasty*) (53) und Brachytherapie (*brachytherapy*) (54) eingeführt. Im Zuge dieser Neuerungen wurde dann der von Grüntzig eingeführte Begriff der perkutanen transluminalen koronaren Angioplastie (*percutaneous transluminal coronary angioplasty, PTCA*) auf perkutane koronare Intervention (*percutaneous coronary intervention, PCI*) geändert.

Obwohl die Grundlagen einer Reihe der Katheter-vermittelten Verfahren, insbesondere der perkutanen Angioplastie (29), der systemischen (55) und selektiven Fibrinolyse (56) sowie des Stentings (57), durch die interventionellen Radiologen zur Behandlung der peripheren arteriellen Verschlusskrankheit gelegt wurden, haben erst die Erfolge der von Grüntzig systematisch entwickelten Methodik der koronaren Dilatationen eine breitere klinische Akzeptanz der perkutanen endoluminalen Gefäßtherapie bewirkt.

Das Prinzip der koronaren Angioplastie nach Grüntzig bestand in vier wesentlichen Arbeitsschritten: dem Legen eines peripheren arteriellen Zugangs nach Seldinger- Methode mittels einer Schleuse, Schaffung eines stabilen Arbeitskanals zwischen arteriellem Zugangsgefäß und dem koronaren Zielgefäß mittels eines Führungskatheters, Ansteuerung des Zielsegmentes mittels eines am Ballonkatheter befestigten Führungsdrahts und der Dilatation der Zielläsion mittels eines am Ende des Katheters befestigten Ballons. Später wurde die koronare Angioplastie nach Grüntzig mehrfach modifiziert, insbesondere wurde die Methodik des kurzen, am Dilatationskatheter befestigten Führungsdrahts verlassen und durch die OTW- und dann die Rx-Technologie ersetzt. Für den Erfolg der koronaren Intervention war die konsequente Optimierung und Weiterentwicklung der mechanischen Eigenschaften einzelner Komponenten und ihrer Synergie im co-axialen Interventionssystem, bestehend aus Schleuse, Führungskatheter, Führungsdraht, Dilatationskatheter bzw. später des Stentträgers, entscheidend. Der industrielle Einsatz modernster Technologien leistete zu Verbesserungen und Verfeinerungen des koronaren Instrumentariums einen entscheidenden Beitrag. Durch Einführung neuer Materialien und Herstellungsverfahren wurden die mechanischen Eigenschaften der traditionellen Instrumente wie Stabilität, Festigkeit, Flexibilität und Gleitfähigkeit weiter optimiert. So wurden beispielsweise in den koronaren Interventionen die bis in die späten 1990-er Jahre üblichen 8F (2.67mm bzw. 0.105“ Zoll) oder 9F (3.0mm bzw.

0.118“ Zoll) Systeme weitgehend durch 5F (1.67mm bzw. 0.065“ Zoll) und 6F (2.00mm bzw. 0.079“ Zoll) Systeme ersetzt. Die konsequente Standardisierung und Weiterentwicklung der koronaren 0.014“ Zoll (0.36mm) Rx- und OTW- Technologie hat die Sicherheit der koronaren Interventionen deutlich verbessert und das Behandlungsspektrum wesentlich erweitert. Zusätzlich konnte die ausgereifte Kathetertechnologie und die klinisch vielfach erprobten koronaren Katheterverfahren sukzessiv auf Behandlungen von nichtkoronaren Gefäßen übertragen werden. Eine aktuelle Übersicht über die Anwendung der Koronartechnik in der Therapie der koronaren und nicht-koronaren Gefäßerkrankungen ist verfügbar (58).

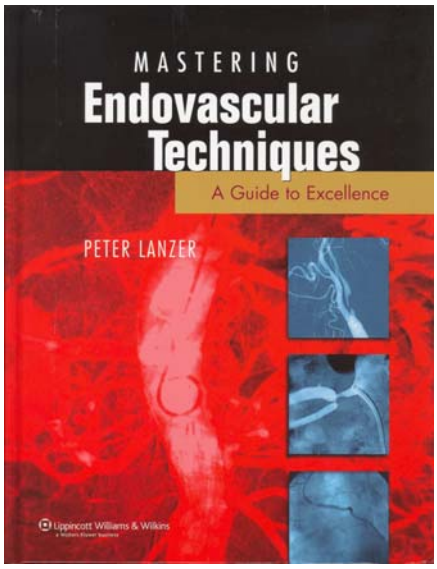

Abbildung 3. Titelseite des Lehrbuchs der endovaskulären Therapien der koronaren und nicht-koronaren Gefäßerkrankungen (58).

Die erfolgreiche Anwendung der Koronartechnik in der Therapie der koronaren und nicht-koronaren Gefäßerkrankungen setzt eine optimale Wahl der Instrumentation und die erforderliche Fachkompetenz der ausführenden Ärzte voraus. Die optimale Wahl der Instrumentation beruht auf der Abstimmung zwischen den biomechanischen Anforderungen des Zielgefäßes und den biomechanischen Möglichkeiten des gewählten Instrumentariums (*matching*) (59). Für die optimale Wahl sind daher gute Kenntnisse der wesentlichen technischen Eigenschaften der einzelnen Instrumente erforderlich. Als klinisch relevante technische Parameter können in-vitro die Vorschubfähigkeit (*pushability*), Steuerbarkeit

(*trackability*), Passagefähigkeit (*crossability*) und Drehfestigkeit (*torque*) der koronaren Kathetersysteme gemessen werden. In ihrer Gesamtheit bestimmen diese Parameter die Fähigkeit der koronaren Kathetersysteme den Zielort zu erreichen (*deliverability*) (60). Für die Qualität der Durchführung der Stentimplantation ist eine Reihe besonderer biomechanischer Eigenschaften wie Radialkraft, radiale Steifigkeit, Stressverhalten und viele andere, verantwortlich (61).

Die interventionelle Fachkompetenz setzt sich aus dem Fachwissen (*knowledge)* und aus einer Reihe von spezifischen Fertigkeiten (*skills*) zusammen. Das Fachwissen hat zwei wesentliche Komponenten (62). Das Fachwissen-Warum (*knowledge-that*) ist deskriptiv und betrifft den gesamten medizinischen, für die Durchführung der Intervention erforderlichen Hintergrund. Das Fachwissen-Wie (*knowledge how*) ist prozedural und betrifft vor allem die praktischen, für die eigentliche Durchführung der Intervention erforderlichen Kenntnisse. Das Fachwissen-Warum wird in der Regel explizit, das Fachwissen-Wie vorwiegend implizit übertragen (63). Die Fertigkeiten sind Ausdruck der Qualität der Umsetzung des interventionellen Wissens in die praktische Tätigkeit während der Intervention (*knowledge in action*); sie sind entweder kognitiv (64) oder psycho-motorisch (65) fundiert. Im Bereich der koronaren Interventionen stellt das Fachwissen-Warum im engeren Sinne die medizinische Begründung und Rechtfertigung der Indikation dar und legt die Rahmenbedingungen für ihre Durchführung fest. Das Fachwissen-Wie im engeren Sinne stellt das Fundament der praktischen Durchführung der Interventionen dar.

Der Erwerb des Fachwissen-Warum ist durch Studium der Fachliteratur möglich, der Erwerb des Fachwissen-Wie beruht traditionell auf Empirie. Die frühere Überzeugung, dass die Länge (in Jahren) der praktischen Erfahrung die Grundlage der fachlichen Qualifikation darstellt, wurde in den 1990-er Jahren eindeutig widerlegt. Es wurde in einer Reihe von Fachdomänen einschließlich der Medizin (66), und dort vor allem in der Chirurgie (67) und in der Anästhesiologie (68), gezeigt, dass das fachliche Können aus der Explikation des Fachwissen-Wie, der gezielten Praxis bestimmter Handlungen (*deliberate practice*) und aus der korrektiven Rückkoppelung (*feed-back*) abgeleitet wird (69).

Die Übertragung des Fachwissens in der koronaren interventionellen Therapie wurde traditionell meist implizit in Wechselwirkung zwischen dem Lernenden und seinem Mentor vorgenommen. Dieser Modus des Wissenstransfers ist in hohem Maße von der

Wahrnehmungsfähigkeit des Lernenden und von der Lehrfähigkeit des Mentors abhängig und daher oft unzuverlässig. Explikation des Fachwissens-Wie erlaubt eine effiziente und konsistente Wissensübertragung; sie ist für eine optimale Prozessqualität der Koronarverfahren in der Therapie der koronaren und nicht-koronaren Gefäßkrankheiten unabkömmlich (70). Eine umfassende Darstellung der expliziten Wissensübertragung in der Katheter-vermittelten kardiovaskulären Therapie wurde im Lehrbuchformat zusammengestellt (Abbildung 4) (71).

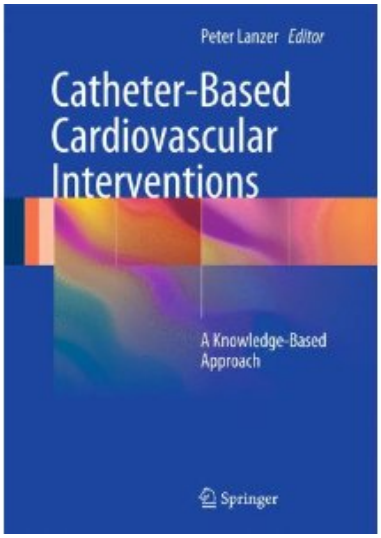

Abbildung 4. Titelseite des Lehrbuchs über die explizite Wissensübertragung in der Katheter-vermittelten kardiovaskulären Therapie (71).

2. Zielsetzung

Das gemeinsame Ziel der vorgelegten Studien war, die Inzidenz der multifokalen klinisch bedeutsamen Atherosklerose als besondere Zielgruppe für Koronarinterventionen in nicht-koronaren Gefäßen zu definieren, die Voraussetzungen der Übertragung der kognitiven Leistungen bei Koronarinterventionen auf die Nicht-koronaren Interventionen zu untersuchen und die Übertragbarkeit der Koronarmethodik auf nichtkoronare Interventionen am eigenen Patientengut zu überprüfen.

Die Patienten mit multifokaler Atherosklerose stellen als potentielle Zielgruppe für koronare Katheter-vermittelte Verfahren zusätzlich eine besondere Risikopopulation dar und sind daher für die Therapieplanung von einer herausragenden Bedeutung. In der verfügbaren Fachliteratur wurde bisher vor allem die Inzidenz der multifokalen Atherosklerose bei Patienten mit peripherer arterieller Verschlusskrankheit untersucht. Das Ziel der ersten Studie war es, die Inzidenz der klinisch relevanten multifokalen Atherosklerose bei Patienten mit primärer koronarer Herzerkrankung zu untersuchen.

Das Ziel der zweiten Studie war, die kognitiven Leistungen bei koronaren Interventionen zu untersuchen und ihre Übertragbarkeit auf Interventionen der nichtkoronaren Gefäße mono- oder multifokaler Genese zu untersuchen.

Das Ziel der dritten und der vierten Studie war die Eignung der Koronartechnik für Revaskularisationen von extrakraniellen Stenosen der Arteria Carotis interna bei Hochrisikopatienten und bei Patienten mit hämodynamisch bedeutsamen Stenosen der Nierenarterien zu untersuchen.

Die Folgestudie hatte zum Ziel die interventionellen Behandlungsmöglichkeiten von Patienten mit einer multifokalen, klinisch bedeutsamen Atherosklerose mittels Simultaninterventionen zu untersuchen.

3. Originalarbeiten

3.1 Vascular multimorbidity in patients with a documented coronary artery disease

2001 wurden 1855 konsekutive Patienten mit koronarangiographisch dokumentierter, hämodynamisch bedeutsamer koronarer Herzkrankheit, KHK, definiert als Angina pectoris in Verbindung mit dem Nachweis einer Myokardischämie oder mindestens einer koronarangiographischen Stenose ≥ 50% des Nominaldurchmessers untersucht. Eine zusätzliche klinisch bedeutsame nichtkoronare Gefäßerkrankung wurde definiert als eine zerebrovaskuläre Erkrankung bei anamnestischer Angabe eines Schlaganfalls oder beim Nachweis einer nach Duplexkriterien ≥50% Stenose der Arteria carotis interna, eine periphere arterielle Verschlusskrankheit beim Nachweis eines Knöchel-Arm-Indexes <0.9 und eine relevante Nierenarterienstenose als eine ≥50% Stenose mindestens einer Nierenarterie in selektiver angiographischer Darstellung. Die KHK war in 31.8% aller untersuchten Patienten mit mindestens einer signifikanten Erkrankung einer weiteren Gefäßregion vergesellschaftet. Am häufigsten war die KHK mit einer klinisch bedeutsamen peripheren arteriellen Verschlusskrankheit kombiniert (n=176; 9.5%). Die zweithäufigste Kombination war KHK und eine zerebrovaskuläre Erkrankung (n=160; 8.6%). Bei 91 (4.9%) Patienten lag gleichzeitig eine klinisch bedeutsame koronare, zerebrovaskuläre und periphere arterielle Erkrankung vor; bei 22 (1.2%) Patienten waren alle vier untersuchten Gefäßbereiche gleichzeitig betroffen. In der univariaten Analyse waren alle untersuchten kardiovaskulären Hauptrisikofaktoren (Diabetes mellitus Typ II, Lipoproteinstoffwechselstörung, arterielle Hypertonie, Rauchen, Alter und familiäre Prädisposition) mit der klinisch bedeutsamen, multifokalen Atherosklerose positiv und signifikant assoziiert. In der multifaktoriellen Analyse blieb eine signifikante Korrelation auf Patienten mit Diabetes mellitus Typ II beschränkt; sie galt sowohl für das Gesamtpatientenkollektiv der Diabetiker als auch für alle untersuchten Altersgruppen (35-54 Jahre, 55-74 Jahre und ≥75 Jahre) bei beiden Geschlechtern. Neben Diabetes war für das Auftreten der klinisch bedeutsamen, multifokalen Atherosklerose bei beiden Geschlechtern das Alter der bedeutendste Risikofaktor.

[*Lanzer P. Vascular multimorbidity in patients with a documented coronary artery disease. ZKardiol 2003;92:650-659*]

3.2. Expanding the base for teaching of percutaneous coronary interventions: The explicit approach

Der formale Ablauf der Katheter-vermittelten koronaren Interventionen wird in fünf Abschnitte eingeteilt. Die *Initiierung* (*initialization*) beginnt mit der Indikationsstellung und endet mit der Intubation des Ostiums des Zielgefäßes. Der wesentliche Bestandteil der Initiierung ist die Aufstellung einer Strategie. Die Strategie legt innerhalb des verfügbaren Entscheidungsraums den Weg vom Befund zum Behandlungsziel fest, sie basiert auf dem Fachwissen und den Fertigkeiten des agierenden Operateurs. Jede Strategie wird durch einen iterativen Entscheidungsprozess motiviert. Die Strategie ist stets patientenspezifisch, ihre Bausteine, genannt interventionelle Module, sind jedoch allgemeingültig. Die drei für den Strategieaufbau entscheidenden Faktoren sind der Zustand des Patienten, die Erreichbarkeit und die biomechanischen Eigenschaften der Zielläsion sowie die aktuell verfügbare Fachkompetenz des Operateurs. Die interventionellen Module als Bausteine der Strategie bestehen jeweils aus vier Schritten: angiographische Darstellung des Interventionssitus, Bildauswertung, Entscheidung und Ausführung der Aktion. Sie sind generisch, d.h. in der jeweiligen Fallgruppe allgemeingültig. Der generische Charakter der interventionellen Module ermöglicht ähnlich den Bausteinen in einem Legospiel ihren Einsatz in unterschiedlichen klinischen Szenarien. Die Aktionen sind entweder diagnostische oder interventionelle Schritte. Mit Ausnahme des in der jeweiligen Intervention letzten Moduls triggert stets jede Aktion den Anfang des Folgemoduls. Die minimale Anzahl der Module, N, in einer Katheter-vermittelten Intervention ist N=2, ihre maximale Zahl kann mehrere Dutzend betragen. Der modulare Ablauf der Katheter-vermittelten Interventionen verleiht der Strategieplanung einen reproduzierbaren algorithmischen Charakter, der für die Ausbildung einer geeigneten interventionellen Heuristik gut geeignet ist.

Bei der Planung und Durchführung einer Katheter-vermittelten Intervention ist die fortlaufende Risikoeinschätzung (*risk accounting*) von zentraler Bedeutung. Qualitativ entspricht das Risiko einem unerwünschten Ereignis, das während einer bestimmten Intervention passieren kann. Quantitativ ist das Risiko das Produkt der Wahrscheinlichkeit des Auftretens eines bestimmten unerwünschten Ereignisses und der Schwere der sich daraus ergebenden Folgen. Die Verwendung des Begriffs des quantitativen Risikos ist in der interventionellen Therapie sinnvoll, obwohl beide, sowohl die Wahrscheinlichkeit des Eintretens des unerwünschten Ereignisses als auch die Schwere der Folgen, im Voraus nicht

genau bestimmbar sind. Um das Gesamtrisiko einer jeden Intervention besser einschätzen zu können, werden zwei grundlegende Risikoarten unterschieden; eine latente (*latent risk*) und eine aktive (*actional risk*) Risikoart. Latentes Risiko ist fallspezifisch und kann aus der Summe der Patienten- und Zielläsion- relevanten Faktoren geschätzt werden. Aktionsrisiko wird weiter in ein Risiko der optimalen Wahl – unvermeidbares Risiko - (*optimum-choice risk*) und ein Risiko suboptimaler Wahl, das sich aus Risiken als Folge von Wissenslücken (*knowledge risk*) und mangelnden Fertigkeiten (*skill risk*) zusammen setzt.

Das latente Risiko ist nicht absolut sondern relativ und dazu noch beweglich; es wird stets durch die Fachkompetenz des Operateurs gewichtet und mit jeder neuen interventionellen Aktion neu definiert. Daher ist es notwendig während einer Intervention das latente Risiko gegen das Aktionsrisiko fortlaufend abzuwägen und das sich dann ergebende Nutzen-Risiko-Verhältnis jeweils zu aktualisieren.

Im *Hauptzyklus* (*main interventional cycle*) wird die Strategie Schritt-für-Schritt definiert. Die Qualität der Strategie entscheidet über den Erfolg in der praktischen Umsetzung. Im Idealfall werden alle durch die Strategie festgelegten interventionellen Module eins-zu-eins umgesetzt. In der Realität der interventionellen Praxis sind jedoch insbesondere in komplexen Fällen perfekte Strategien eher selten; vielmehr werden in der Durchführung öfter von der Strategie abweichende Schritte erforderlich. Die Summe der Abweichungen wird als Taktik bezeichnet, die geänderten interventionellen Module sind Improvisationen. In der Regel ist das Gesamtrisiko einer Strategie-motivierten Intervention am niedrigsten; das höchste Gesamtrisiko ist in der Regel bei weitgehend improvisierten Interventionen zu erwarten.

Die Terminierung (*termination*) beginnt mit Entfernung der Instrumente aus dem Gefäßsystem und endet mit dem Verschluss des arteriellen Zugangs, der Hämostase. Nachsorge (*aftercare*) und Verlaufskontrollen (*follow-up*) schließen sich der interventionellen Behandlung an und werden zeitlich unterschiedlich definiert; beispielsweise endet die Nachsorge mit der Entlassung des Patienten und die Verlaufskontrollen werden sechs Monaten nach der Entlassung aus dem Krankenhaus beendet. Nach Erwerb der Kenntnisse über den formalen Ablauf der Katheter-vermittelten Interventionen werden die kognitiven Fähigkeiten und die manuellen Fertigkeiten der Operateure ausgebildet. Zu den elementaren jedoch hochkomplexen kognitiven Fähigkeiten gehört vor allem eine präzise, effiziente und konsistente Interpretation der statischen und dynamischen Angiogramme in Echtzeit; auch bei

Stressbelastungen und unter Zeitdruck. Die genaue Einschätzung der biomechanischen Eigenschaften der behandelten Gefäßregionen einschließlich der Zielläsionen und die Abstimmung (*matching*) zwischen mechanischen Anforderungen des interventionellen Situs und der technischen Eigenschaften der Instrumente gehören ebenfalls dazu. Diese hochkomplexen kognitiven Fähigkeiten sind Ausdruck einer Vielzahl von untergeordneten kognitiven Ressourcen wie Merkfähigkeit, Konzentration, Aufmerksamkeit, Abrufvermögen und weiteren Eigenschaften wie Stressfestigkeit, Ausdauerfähigkeit, Vorurteilsresistenz und anderen. Diese generischen kognitiven Fähigkeiten sind bei allen Katheter-vermittelten Interventionen anwendbar und werden dann durch ein Gefäßregion-spezifisches Wissen-Warum und Wissen-Wie ergänzt. Die Effizienz und die Zuverlässigkeit des Erwerbs von neuen kognitiven Fähigkeiten durch explizites Lernen sind deutlich höher als bei impliziter Wahrnehmung**.**

Ähnlich wie im Falle der kognitiven Fähigkeiten wird bei den Katheter-vermittelten Interventionen ebenfalls eine ganze Reihe von generischen technischen Fertigkeiten (*skills; knowledge in action*) benötigt. Die sichere Beherrschung der manuellen Fertigkeiten wird durch genaue verbale bzw. graphische Handlungsanweisungen bezüglich einzelner Schritte gefestigt und beschleunigt. Das interventionelle Wissen-Wie in Form von kognitiven Fähigkeiten und manuellen Fertigkeiten wird somit am effektivsten durch verbale Explikation, aktives Vormachen und gezieltes Nachmachen übertragen.

Mittels einer Computersimulation wurden anhand einer vereinfachten, aus vier Aktionen bestehenden Intervention die Unterschiede im Entscheidungsverhalten zwischen einem erfahrenen, weniger erfahrenen und unerfahrenen Untersucher dargestellt. Aufgrund des formal ähnlichen Aufbaus sind die kognitiven Anforderungen an die im Bereich der Koronargefäße behandelnden Ärzte mit den kognitiven Anforderungen an die Untersucher in anderen Gefäßregionen ähnlich zu bewerten.

[*Lanzer P, Prechelt L. Expanding the base for teaching of percutaneous coronary interventions: The explicit approach. Cath Cardiovasc Interv 2011;77:372-380*]

3.3. Carotid-artery stenting in a high-risk patient population – single centre, single operator results

In eigener Untersuchungsreihe wurden 143 konsekutive Patienten, davon 100 Männer und 43 Frauen mit mittlerem Alter von 68.7± 8.0 Jahren und Nachweis einer hämodynamisch bedeutsamen Karotisstenose (definiert als Stenose >70% des nominalen Gefäßdurchmessers bei symptomatischem und Stenose >80% bei asymptomatischem Verlauf) perkutan mittels der koronaren Technologie und Interventionstechnik behandelt. Die koronare Methodik und das koronare Interventionsprinzip wurde durch die Anwendung folgender Instrumentation definiert: 6F (Frenchgröße) 90cm lange Einführungsschleuse in Verbindung mit einem 5F diagnostischen Koronarkatheter, oder ein 7F oder 8F koronarer Führungskatheter, ein 0.014“ Zoll koronarer Führungsdraht, ein Rx- Dilatationskatheters und ein Stentträgersystem mit einem sehr niedrigen Profil. In 96 Patienten wurde zusätzlich ein Thromboembolieschutzsystem eingesetzt. Technischer Erfolg, definiert als morphologisch vollständige Beseitigung der Stenose, wurde bei allen behandelten Patienten erreicht. Neurologische Komplikationen traten bei 3.5% der Patienten auf, davon waren 2.1% transitorisch ischämische Attacken (TIA) oder prolongiertes neurologisches Defizit (PRIND) und 1.4% Schlaganfall. Tod trat bei keinem der Patienten auf. Die neurologischen Komplikationen traten häufiger bei Patienten mit symptomatischen Karotisstenosen (2.7% vs. 1.9% asymptomatische Karotisstenosen) auf und sie waren häufiger bei Interventionen ohne Einsatz der Thromboembolieschutzsysteme (TIA/PRIND 4.3% vs. 1.0% und Schlaganfall 2.1% vs. 1.0%). Lokale Komplikationen wurden bei 4.2% der behandelten Patienten beobachtet, davon waren 3.5% Leistenhämatome ohne Notwendigkeit einer Bluttransfusion und 0.7% Pseudoaneurysmen. Zusammenfassend wurde festgestellt, dass die koronare Technologie und Interventionstechnik für die interventionelle Behandlung von Patienten mit Karotisstenosen optimal geeignet ist und vertretbare, der chirurgischen Therapie mindestens vergleichbare Komplikationsraten aufweist.

[*Lanzer P, Weser R, Prettin C. Carotid-artery stenting in a high-risk patient population – single centre, single operator results. Clin Res Cardiol 2006; 95:4–12*]

3.4. Coronary-like revascularization for atherosclerotic renal artery stenosis – Results in 181 consecutive patients

In eigener Untersuchungsreihe wurden 181 konsekutive Patienten, davon 102 Männer im mittleren Alter von 66.1± 9.2 Jahren und 79 Frauen im mittleren Alter von 68.4±9.2 Jahren und Nachweis einer hämodynamisch bedeutsamen Nierenarterienstenose (definiert als Stenose >50% des nominalen Gefäßdurchmessers) perkutan mittels der koronaren Technologie und Interventionstechnik behandelt. Die koronare Methodik wurde durch die Verwendung einer 6F Einführungsschleuse, eines speziellen oder eines koronaren (JR, Judkins rechts oder IMA, internal mammary artery) 6F Führungskatheters, eines 0.014“ Zoll Koronardrahts, eines Rx- Dilatationskatheters und eines Stentträgersystems definiert. Die Interventionen wurden in der Regel als direktes Stenting durchgeführt. Der durchschnittliche Stenosegrad vor Dilatation war 81.3±9.6%; 68.2% der Nierenarterienstenosen waren ostial, in 9.4% lag eine bilaterale Nierenarterienstenose vor. Technisch erfolgreiche Intervention, definiert als residuale Stenose < 30%, wurde in 98.3% der Patienten und 98.5% der Läsionen erreicht. Bei einem Patienten konnte die Zielläsion nicht passiert werden, bei zwei Patienten war der residuale Stenosegrad >30%. Bei keinem Patienten traten schwere kardiovaskuläre Komplikationen, definiert als Tod, Organverlust oder Notoperation, auf. Bei 3.9% der Patienten traten lokale Komplikationen auf; in 2.2% handelte es sich um Hämatome, in 1.7% um Pseudoaneurysmata. Zusammenfassend wurde festgestellt, dass die koronare Methodik und Interventionstechnik für die interventionelle Behandlung von Patienten mit Nierenarterienstenosen gut geeignet ist und insgesamt ein niedriges Interventionsrisiko aufweist.

[*Lanzer P, Weser R, Prettin C. Coronary-like revascularization for atherosclerotic renal artery stenosis – Results in 181 consecutive patients. Clin Res Cardiol 2006; 95:1–7*]

3.5. Intentional single-stage revascularization of two different vascular beds in patients with vascular multimorbidity; Clinical feasibility study

In der Studie wurden 50 nichtkonsekutive Patienten, davon 28 Männer im mittleren Alter von 68.6± 9.2 und 22 Frauen im mittleren Alter von 72.2± 6.4 Jahren, mit Nachweis einer hämodynamisch (Stenose >50% des Nominaldurchmessers der koronaren und nichtkoronaren Arterien, außer der Arteria carotis interna, Stenose der Arteria carotis interna >70% des Nominaldurchmessers) und klinisch bedeutsamen (symptomatischen) mehrortigen Gefäßerkrankung perkutan mittels der koronaren Technologie und Interventionstechnik behandelt. Die koronare Methodik und das koronare Interventionsprinzip wurden durch die Anwendung einer 6F Einführungsschleuse, eines präformierten koronaren Führungskatheters, eines 0.014“ Zoll koronaren Führungsdrahts, eines Rx- Dilatationskatheters und eines Stentträgersystems definiert. Als mehrortige Interventionen in gleicher Sitzung wurden Koronarintervention kombiniert mit Intervention an Nierenarterien (40% der Patienten), Koronarintervention kombiniert mit Intervention an Beinarterien (34% der Patienten), Koronarintervention kombiniert mit Intervention an der Arteria carotis interna (20% der Patienten), Koronarintervention kombiniert mit Intervention an der Nierenarterie und Beinarterie, Intervention an den Beinarterien kombiniert mit Intervention an der Arteria carotis interna und Intervention an den Beinarterien kombiniert mit Intervention an der Nierenarterie (jeweils 2%) durchgeführt. Technischer Erfolg, definiert als Reststenose <30% des Nominaldurchmessers und Abwesenheit von relevanten kardiovaskulären Komplikationen (Major Cardiac and Cerebrovascular Events, MACCE) wurde bei allen behandelten Patienten erreicht. Bei 4.0% der Patienten wurde eine chirurgische Revision der Punktionsstelle erforderlich. Bei 4.0% der Patienten traten Leistenhämatome ohne Notwendigkeit einer Bluttransfusion auf. Im Rahmen dieser Durchführbarkeitsstudie wurden weitere relevante Daten im Bezug auf den zeitlichen Aufwand, Strahlendosis und Kontrastmittelverbrauch ermittelt.

[*Lanzer P, Weser R, Prettin C. Intentional single-stage revascularization of two different vascular beds in patients with vascular multimorbidity; Clinical feasibility study. Clin Res Cardiol 2007;96:1-5*]

4. Diskussion

Aus der Betrachtung der Atherosklerose als einer vaskulären Systemerkrankung wird das Konzept der klinisch relevanten multifokalen Atherosklerose abgeleitet. In der vorgelegten Studie konnte gezeigt werden, dass bei Patienten mit koronarer Herzkrankheit und Indikation zu einer Revaskularisationstherapie definitionsmäßig eine multifokale, klinisch bedeutsame Atherosklerose in 31.8% der untersuchten Patienten vorhanden war. Die klinisch bedeutsame koronare Herzkrankheit war am häufigsten mit einer peripheren arteriellen Verschlusskrankheit vergesellschaftet (9.5%). Das Risiko an einer klinisch relevanten multifokalen Atherosklerose zu erkranken stieg mit dem Alter an. Im multivariaten Modell war jedoch der Diabetes mellitus Typ II als einziger unabhängiger Risikofaktor identifiziert und das erhöhte Risiko war in allen untersuchten Altersgruppen erkennbar. In Anbetracht der demographischen Verschiebung und der steigenden Prävalenz von Typ II Diabetes in Deutschland und in den Industrienationen kann aufgrund der erhobenen Daten von einer stetigen Zunahme der klinisch relevanten multifokalen Atherosklerose ausgegangen werden. Desweiteren ist im Zuge dieser Entwicklung mit weiterer Zunahme der Inanspruchnahme der Katheter-vermittelten Verfahren zu rechnen. Abgesehen von den medizinischen Aspekten ist auch nach den wirtschaftlichen Gesichtspunkten ein optimaler Einsatz der Katheter-vermittelten Therapien zwingend erforderlich.

Der optimale Einsatz der Katheter-vermittelten Therapien erfordert die Verfügbarkeit einer technologisch ausgereiften Instrumentation und die Verfügbarkeit von fachkompetenten, in den interventionellen Verfahren gut ausgebildeten Ärzten. Die koronaren Interventionen sind heute das am besten ausgereifte und bei weitem am häufigsten angewandte Katheter-vermittelte Verfahren. Der Einsatz der modernen Technologie hat über die Jahrzehnte zur Entwicklung eines hochwertigen und leistungsfähigen Instrumentariums geführt und zu der Sicherheit und Effizienz der koronaren Behandlungen beigetragen. Der häufige klinische Einsatz der koronaren Interventionen hat zudem die Ansammlung eines enormen Wissensvorrats über die operativen Möglichkeiten und Grenzen dieses endovaskulären Verfahrens ermöglicht. Die Explikation und der Transfer dieses Wissensvorrats ist für die Weiterentwicklung der Fachkompetenz entscheidend, zumal aufgrund der Grundähnlichkeit der kognitiven Leistungen in allen Katheter-vermittelten Verfahren seine Übertragung auf Behandlungen von nicht-koronaren Gefäßen von besonderem Interesse ist. In der vorgelegten Studie wurde der formale iterative Prozess der Koronarinterventionen dokumentiert und als

Modell einer Katheter-vermittelten Intervention schlechthin definiert. Im Weiteren wurden die entscheidenden kognitiven Leistungen, insbesondere in Bezug auf Entscheidungsfindungen beschrieben und anhand eines Computermodells abgebildet. Dabei wurde die grundlegende Bedeutung der Risikoabwägung in den Entscheidungsprozessen analysiert. Im Rahmen der Arbeit wurde gezeigt, dass die Explikationen der formalen und kognitiven interventionellen Prozesse unter Umständen eine deutliche Steigerung der Effizienz der Wissensübertragung ermöglicht und die Grundlage für eine gezielte praktische Ausübung der interventionellen Tätigkeit darstellen könnte.

Aufgrund der Ähnlichkeiten des formalen Aufbaus und aufgrund der Vergleichbarkeit der kognitiven Anforderungen erscheint der Einsatz der Methodik der koronaren Interventionen in nicht-koronaren Gefäßbereichen zumindest theoretisch möglich. Der dadurch realisierte Wissenstransfer sollte den Lernprozess verkürzen und die Aufnahmefähigkeit für gefäßspezifische Besonderheiten verbessern. In der Tat wurden beispielsweise in der „Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) Studie“ signifikante Unterschiede in den Ergebnissen der Katheter-vermittelten Carotisinterventionen demonstriert, wenn die Daten nach Berufsgruppen (Kardiologen, Gefäßchirurgen) analysiert wurden (unveröffentlichte Daten). In den vorliegenden Studien wurde die Methodik der koronaren Interventionen bei Risikopatienten mit signifikanten, symptomatischen und asymptomatischen Stenosen der Carotis interna und bei Patienten mit hämodynamisch bedeutsamen Stenose der Nierenarterien eingesetzt und ausgewertet. Die Auswertung beider Studien zeigte überzeugend, dass nach entsprechender Einarbeitung in die Besonderheiten beider behandelten Gefäßbereiche, insbesondere in Bezug auf den Zugang zum Zielgefäß, Platzierung eines Thromboembolieschutzsystems und Freisetzung einer selbstexpandierenden Gefäßstütze (Carotis interna) und in Bezug auf die Drahtführung in einem Parenchymorgan und Platzierung der Gefäßstütze im Bereich des Ostiums bei unterschiedlichen Zugverhältnissen (Nierenarterien), die in Koronarinterventionen erfahrenen Ärzte ohne langfristige Zusatzausbildung sehr gute klinische Ergebnisse in interventionellen Behandlungen erreichen können.

Im Rahmen einer weiteren Studie konnte gezeigt werden, dass Ärzte mit Erfahrungen in interventionellen Behandlungen in unterschiedlichen Gefäßregionen mittels der Koronarmethodik mit ihren gefäßspezifischen Abwandlungen durchaus in der Lage sind, Behandlungen verschiedener Gefäßbereiche in einer Sitzung vorzunehmen, ohne dass das für

die monoterritoreale Interventionen bekannte Eingriffsrisiko, mit möglicher Ausnahme der lokalen Komplikationen des arteriellen Zugangs, erhöht wird. Bei Patienten mit multifokaler, klinisch bedeutsamer und behandlungsbedürftiger Atherosklerose bieten somit die Simultaninterventionen im Vergleich zur Durchführung von Eingriffen in getrennten Sitzungen insgesamt eine Risikoreduktion. Im Weiteren konnte durch die Simultaninterventionen im Vergleich zu getrennt durchgeführten Interventionen die Eingriffszeit verkürzt und dadurch die Gesamtbelastung der Patienten reduziert werden.

5. Zusammenfassung und Ausblick

Fachkompetenz in der Durchführung von Koronarinterventionen wird durch Explikation des Fachwissen-Wie und gezielte Praxis gefördert und weiter ausgebaut. Aufgrund der vergleichbaren kognitiven und technischen Grundanforderungen bei interventionellen Eingriffen in unterschiedlichen Gefäßregionen wird der Transfer von den bei koronaren Interventionen benötigten Fähigkeiten und Fertigkeiten auf die Katheter-vermittelten Behandlungen an nichtkoronaren Gefäßen deutlich erleichtert. Die Fortschritte und die schnelle Entwicklung in der Methodik und Technologie der koronaren Interventionen begünstigen zusätzlich den Wissenstransfer auf interventionelle Behandlungen anderer Gefäßregionen. Die bisherigen Erfahrungen zeigen, dass die koronaren Verfahren eine wichtige methodische und technische Grundlage für Behandlungen einer Reihe von nichtkoronaren Erkrankungen liefern. Diese Verfahren sind für die Simultaninterventionen an Gefäßen unterschiedlicher Regionen und für die kombinierten interventionellen und operativen Hybridinterventionen gut anwendbar. In Anbetracht des stattfindenden demographischen Wandels sowie der ansteigenden Prävalenz des Typ II Diabetes in Deutschland und den Industrienationen sind eine zunehmende Inzidenz der multifokalen Atherosklerose und steigender Bedarf an kardiovaskulärer interventioneller Fachkompetenz zu erwarten.

6. Literaturverzeichnis

1. McGill H Jr. (ed). The geographic pathology of atherosclerosis. Lab Invest 1968;18:465-639

2. Atherosclerosis of the aorta and coronary arteries in five towns. Bulletin World Health Organisation, Geneve. 1976, Seiten 485-638

3. Stary HC. Evolution and progression of atherosclerotic lesions in coronary arteries of children und young adults. Atherosclerosis Suppl I,1989;9:I-19-I-32

4. Stary HC, Chandler AB, Dinsmore RE et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis; A report from the committee on Vascular Lesions of the Council on Atherosclerosis, American Heart Association. Arterioscler Thromb Vasc Biol 1995;15:1512-31

5. Bates SR, Gangloff ED (eds). Atherosclerosis and aging. New York:Springer,1985.

6. Woolf N. Pathology of atherosclerosis, London; Butterworth, 1982

7. Hopkins PN, Williams RR. A survey of 246 suggested coronary risk factors. Atherosclerosis 1981;40:1-52

8. Kannel WB. Bishop lecture. Contribution of the Framingham Study to cardiology. J Amer Coll Cardiol 1990;15:206-211

9. Averbook A, Wilson SE, White GH. Etiology and anatomic distribution of atherosclerosis in man. In: White RA (ed). Atherosclerosis and arteriosclerosis: human pathology and experimental animal methods and models. Boca Raton (Florida): CRC Press, 1989, pp. 17-48

10. Ghazalpour A, Doss S, Aten J, Toomey EM, Van Nas A, Wang S, Drake TA, Lusis AJ. Toward a biological network of atherosclerosis. J Lipid Res 2004;45:1793-1805

11. Ross R. Atherosclerosis – an inflammatory disease. N Engl J Med 1999;340:115-126

12. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316:1371-1375

13. Chandler AB, I Chapman, LR Erhardt, WC Roberts, CJ Schwartz, D Sinapius, DM Spain, S Sherry, PM Ness, TL Simon: Coronary thrombosis in myocardial infarction. Report of a

workshop on the role of coronary thrombosis in the pathogenesis of acute myocardial infarction. Am J Cardiol 1974; 34:823-833

14. Falk E Why do plaques rupture? Circulation 1992;86 (Suppl III):III30-III42

15. BraunwaldE. Efforts to limit myocardial infarct size: historical considerations. Eur Heart J. 1985;6:E1–E4

16. Rentrop P, Blanke H, Karsch KR, Kaiser H, Koestering H, Leitz K Selective intracoronary thrombolysis in acute myocardial infarction and unstable angina pectoris. Circulation 1981: 63:307-317

17. Schröder R, G Biamino, L Enz-Rudiger. Intravenous short- term infusion of streptokinase in acute myocardial infarction. Circulation 1983; 63:536-48

18. Hartzler GO, Rutherford BD, McConahay DR. Percutaneous transluminal coronary angioplasty: application for acute myocardial infarction. Am J Cardiol 1984;53:117C-121C

19. Lanzer P, Zuehlke H, Jehle P, Silber R-E Cardiovascular multimorbidity, emerging coalescence of the integrated panvascular approach. Z Kardiol 2004;93:259-265

20. Lanzer P, Topol EJ (Hrsg.) PanVascular medicine; integrated clinical management. Springer: New York, Berlin, 2002

21. Long ER The development of our knowledge of arteriosclerosis. In: Cowdry EV (Hrsg.) Arteriosclerosis; A survey of the problem. New York: McMilllan Co. 1933;S.19-52

22. Hertzer NR, Beven EG, Young JR, O'Hara PJ, Ruschhaupt WF, Graor RA; DeWolfe VG, Malovec LC. Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. Ann Surg 1984;199:223-233

23. Hertzer NR, Young JR, Beven EG, Graor RA; O'Hara PJ, Ruschhaupt WF 3rd, DeWolfe VG, Malovec LC. Coronary angiography in 506 patients with extracranial cerebrovascular disease. Arch Int Med 1985;145:849-852

24. DeBakey ME, Lawrie GM, Glaeser DH. Patterns of atherosclerosis and their surgical significance. Ann Surg 1985;201:115-131

25 CAPRIE steering committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischemic events. Lancet 1996;348:1329-39

26. Bhatt DL, Peterson ED, Harrington RA, Ou FS, Cannon CP, Gibson CM, Kleinman NS, Brindis RG, Peacock WF, Brener SJ, Menon V, Smith SC Jr, Pollack CV Jr, Gibler WB, Ohman EM, Roe MT, CRUSADE Investigators. Prior polyvascular disease: risk factor for adverse ischaemic outcomes in acute coronary syndromes. Eur Heart J 2009;30:1195-1202

27. Diehm C, Schwertfeger M, Pittrow D. Substanzielle Komorbidität von Manifestationen der Atherothrombose. Herzmed 2008;25:6-13

28.Seldinger SI. Catheter placement of the needle in percutaneous arteriography. Acta Radiol [Diagn] (Stockh] 1953;39:368-376.

29. Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction. Description of a new technic and a preliminary report of its application.Circulation 1964;30:654-670.

30. Portsmann W. Ein Neuer Korsett-Ballonkatheter zur Transluminalen Rekanalisation nach Dotter unter besonderer Berücksichigung von Obliterationen an den Beckenarterien. Radio. Diagn (Berl.), 1973;14:239-244.

31. Grüntzig A, Hopf H. Perkutane Rekanalisation chronischer Verschlüsse mit einem neuen Dilatationskatheter: Modifikation der Dotter-Technik. Dtsch Med Wschr 1974;99:2502-05.

32. Grüntzig A, Leu HJ, Asher A. Mechanische Rekanalisation künstlicher Thromben der Arteria femoralis beim Hund. 6. Jahrestagung der Österreichischen Gesellschaft für Gefäßchirurgie, Klagenfurt 1973. Basel: Krager, 1975:207-213.

33. Grüntzig A, Die perkutane Rekanalisation chronischer arterieller Verschlüsse mit einem neuen doppellumigen Dilatationskatheter. Fortschr Röntgenstr 1976;124:80-86.

34. Grüntzig A, Vetter W, Meier M, Lütolf U, Siegenthaler W. Treatment of renovascular hypertension with percutaneous transluminal dilatation of renal artery stenosis. Lancet 1978;i:801-2.

35. Grüntzig A, Gleichner H. US Patent 4195637 - Catheter arrangement, method of catheterization, and method of manufacturing a dilatation element. http://www.patentstorm.us/patents/4195637/fulltext.html.

36. Grüntzig A. Perkutane Dilatation von Koronarstenosen. Beschreibung eines neuen Kathetersystems. KlinWschr 1976;124:543-545.

37. Grüntzig A, Riedhammer HH, Turina M, Rutishauser W. Eine neue Methode zur perkutanen Dilatation von Koronarstenosen. Tierexperimentelle Prüfung. Verh Dtsch Ges Kreisl Forsch 1976;42:282-5

38. Grüntzig A, Schneider J. Die perkutane Dilatation chronischer Koronarstenosen – Experiment und Morphologie. Schweiz Med Wschr 1977;107:1588

39. Grüntzig A, Myler R, Hanna ES, Turina M. Coronary transluminal angioplasty. Circulation 1977;56(Abstract):84

40. Grüntzig A. Transluminal dilatation of coronary artery stenosis (letter). Lancet 1978, 1(8058):263

41. Grüntzig A, A Senning A, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. N Engl J Med. 1979;301:61-68

42. Grüntzig A. PTCA Technique with a Double Lumen Dilatation Catheter. Proc Workshop Percutaneous Transluminal Coronary Angioplasty, NIH. 1980; Publication No. 80-2030:123-133

43. Simpson JB, Baim DS, Robert EW, Harrison CD. A new catheter system for coronary anagioplasty. Am J Cardiol 1982;49:1216-1222

44. Kaltenbach M. The long wire technique – a new technique for steerable balloon catheter dilatation of coronary artery stenoses. Eur Heart J 1984;5_1004-1009

45. Nordenström B. Balloon catheters for percutaneous insertion into the vascular system. Acta Radiol 1962;57:411-416

46. Bonzel T, Wollschläger H, Just H. Ein neues Kathetersystem zur mechanischen Dilatation von Koronarstenosen mit austauschbaren intrakoronaren Kathetern, höherem Kontrastmittelfluss und verbesserter Steuerbarkeit. Biomed Tech 1986;31:195-200

47. Yock P. Angioplasty apparatus facilitating rapid exchanges. US- patent no. 5,061,273, Issued October 29, 1991

48. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. New Engl J Med 1987;316:701-6

49. Puel J, Joffre F, Rousseau F. Endo-protheses coronariennes auto-expansive dans le prevention des restenoses apres angioplastie transluminale. Arch Mal Couer 1987;8:1311-1312

50. Sousa JE, Costa MA, Abizaid A, Abizaid AS, Feres F. Pinto IMF, Seixas AC, Staico R, Mattos LA, Sousa GMR, Falotico R, Jaeger J, Popma JJ, Serruys PW. Lack of neointimal proliferation after implantation of sirolimus-coated stents in human coronary arteries; a quantitative coronary angiographry and three-dimensional intravascular ultrasound study. Circulation 2001;103:192-195

51. Simpson JB, Johnson DE, Thapliyal HV, Marks DS, Braden LV Transluminal atherectomy: A new approach to the treatment of atherosclerotic vascular disease. Circulation 72 (Suppl II):111-146 (abstract)

52. Kensey KR, Nash JE, Abrahams L, Zarius CK Recanalization of obstructed arteries with a flexible, rotating tip catheter Radiology. 1987,165:387-389

53. Litvack F, Grundfest W, Hickey A, Jakubovski A, Mohr F, Segalowitz J, Hestrin F, Goldenberg T, Laudenslager J, Narciso H, Forrester S Percutaneous coronary excimer laser angioplasty in animals and humans. J Am Coll Cardiol 1989;13:61A

54. Teierstein PC, Massullo V, Jani S et al. Catheter-based radiotherapy to inhibit restenosis after coronary stenting. N Engl J Med 1997;336:1697-1703

55. Dotter CT, Rösch J, Seaman AJ, Dennis D, Massey WH. Streptokinase treatment of thromboembolic disease. Radiology 1972;102:283–90

56. Dotter CT, Rosch J, Seaman AJ. Selective clot lysis with low-dose streptokinase. Radiology 1974;111:31–7

57. Dotter CT, Buschmann PAC, McKinney MK, Rosch J. Transluminal expandable nitinol coil stent grafting: preliminary report. *Radiology*.. 1983;147:259-260

58. Lanzer P (Hrsg.). Mastering endovascular interventions; Guide to excellence. Philadelphia: Lippincott, Williams & Wilkins, 2006

59. Lanzer P, Gijsen FJH, Topoleski LD, Holzapfel GA. Call for standards in technical documentation of intracoronary stents. Herz 2010;35:27-33

60. Schmidt W, Lanzer P, Behrens P, Topoleski T, Schmitz K-P. A Comparison of the mechanical performance characteristics of seven drug eluting stents. Cath Cardiovasc Interv 2009;73:350-360

61. Guidance for industry and FDA staff non-clinical engineering tests and recommended labeling for intravascular stents and associated delivery systems. http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm071863.htm (01.04.2012)

62. Ryle G. The concept of mind. London: Hutchinson's University Library, 1949.

63. Polanyi M. Personal knowledge; Towards a post-critical philosophy, Chicago: The University of Chicago Press, 1958

64. Gonzalez C. Cognitive science: An introduction. In Lanzer P (ed.) Catheter-based cardiovascular interventions; Knowledge-based approach. Heidelberg: Springer Verlag, 2012 (im Druck)

65. Bock O, Dubrowski A. Psychomotor skills. In Lanzer P (ed.) Catheter-based cardiovascular interventions; Knowledge-based approach. Heidelberg: Springer Verlag, 2012 (im Druck)

66. Ericsson KA (ed.). Development of professional expertise. Cambridge: Cambridge University Press; 2009

67. Tirapille LA. The effect of cognitive task analysis based instruction on surgical skills expertise and performance. Dissertation presented to the Faculty of the USC Rossier School

of Education University of Southern California, in partial fulfillment of the requirements for the Degree of Doctor of Education 2010 (unveröffentlicht)

68. Sullivan ME, Brown CV, Peyre SE, Salim A, Martin M, Towfigh S, Grunwald T. The use of cognitive task analysis to improve the learning of percutaneous tracheostomy placement. Am J Surg 2007;193:96-99

69. Ericsson KA, Krampe RTh, Tesch-Römer C. The role of deliberate practice in the acquisition of expert performance. Psychol Rev 1993;100:363-406

70. Lanzer P, Prechelt L. On acquiring decision making skills for endovascular interventions. EuroIntervention 2008;4:303-305

71. In Lanzer P (Hrsg.) Catheter-based cardiovascular interventions; Knowledge-based approach. Heidelberg: Springer Verlag, 2012 (im Druck)

An den Dekan der Medizinischen Fakultät der
Martin-Luther-Universität Halle
Prof. Dr. med. Michael Gekle

Eidesstattliche Erklärung

Ich versichere, die vorliegende Habilitationsschrift mit dem Thema:

Koronare Interventionen in der Therapie der multifokalen Atherosklerose

als auch die eingereichten wissenschaftlichen Arbeiten ohne fremde Hilfe und ohne andere als die darin angegebenen Hilfsmittel angefertigt zu haben.

Halle, 13.06.2013

Dr. Peter Lanzer

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Vascular multimorbidity in patients with a documented coronary artery disease

Gefäßmultimorbidität bei Patienten mit dokumentierter koronarer Herzerkrankung

Zusammenfassung Atherosklerose ist eine systemische Gefäßerkrankung mit häufig vorkommendem gleichzeitigen Befall von mehreren Gefäßbereichen. Um die Prävalenz und die topographische Verteilung der nichtkoronaren Atherosklerose in den peripheren (PAD), zerebralen (CVD) und renalen (RAD) Arterien bei Patienten mit koronarangiographisch dokumentierter koronaren Herzerkrankung (CAD) zu untersuchen, wurde an wegen Verdacht auf koronare Herzerkrankung stationär eingewiesenen Patienten eine Querschnittsstudie durchgeführt. Zusätzlich wurde der Zusammenhang zwischen der koronaren Herzerkrankung, dem multiterritorialen Gefäßbefall und den Hauptrisikofaktoren untersucht.

1855 konsekutive Patienten, mittleres Alter 65 ± 10,6 Jahre (18–92 Jahre), 1184 (63,8%) Männer und 671 (36,2%) Frauen mit angiographisch nachgewiesener CAD wurden untersucht. Die Patienten wurden in vier Gruppen eingeteilt: Gruppe A < 35 Jahre, Gruppe B 35–54 Jahre, Gruppe C 55–74 Jahre und Gruppe D ≥ 75 Jahre. 1265 (68,2%) der Patienten hatten keine Evidenz für eine relevante nichtkoronare Gefäßerkrankung. Dagegen wurde bei 590 (31,8%) eine signifikante nichtkoronare Gefäßerkrankung mindestens in einer zusätzlichen arteriellen Strombahn dokumentiert. CAD war am häufigsten mit der PAD assoziiert (n = 176; 9,5%). In 22 (1,2%) der Patienten wurden alle untersuchten Gefäßstrombahnen signifikant betroffen. Die Prävalenz der multiterritorialen Gefäßerkrankung nahm mit dem Alter zu, sie war am niedrigsten in der Gruppe A und am höchsten in der Gruppe D. Im Gegensatz zum Gesamtkollektiv wurde bei Frauen die CAD sowohl mit der PAD als auch mit der RAD in der Gruppe B am häufigsten dokumentiert. In der multiplen Regressionsanalyse wurde Typ 2 Diabetes mellitus als einziger unabhängiger Risikofaktor der Gefäßmultimorbidität ermittelt.

Schlüsselwörter
Koronare Herzerkrankung – Gefäßmultimorbidität – Kardiovaskuläre Risikofaktoren

Summary Atherosclerotic artery disease is a systemic vascular disorder typically involving multiple vascular territories in the same patient. To assess the prevalence and the topographic distribution of non-coronary peripheral artery disease (PAD), cerebrovascular (CVD) and renal artery disease (RAD) in patients with an angiographically confirmed coronary artery disease (CAD) a cross-sectional survey among inpatients admitted for symptoms of CAD was performed. The relationship between CAD and multiterritory vascular disease, and the major risk factors were also assessed. A total of 1855 consecutive patients, mean age 65 ± 10.6 years (18–92 years), 1184 (63.8%) men and 671 (36.2%) women with an angiographically confirmed CAD were studied. The patients were divided into four age groups: group A < 35 years of age, group B 35 to 54 years, group C 55 to 74 years and group D ≥ 75 years of age. While 1265 (68.2%) had no evidence of a relevant non-coronary artery disease, in 590 (31.8%) a significant non-coronary artery disease in at least one additional major vascu-

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lar territory was documented. CAD was most frequently associated with PAD in n = 176 (9.5%) patients. In 22 (1.2%), all four studied vascular territories were significantly diseased. The prevalence of the multi-territory artery disease increased with age: lowest in group A and highest in the group D. However, the data analysis by gender revealed the highest prevalence of CAD associated with PAD and RAD, respectively, in women 35 to 54 years of age. Using the multivariant logistic regression model, type II diabetes was the only major risk factor for a multi-territory expression of atherosclerosis.

Key words
Coronary artery disease – vascular multimorbidity – cardiovascular risk factors

Introduction

Atherosclerosis is a systemic disease of the large and medium size arteries associated with disseminated lesions, thromboembolic complications and generalized endothelial dysfunction (1–5). However, as stated by McGill more than thirty years ago "*The severity of atherosclerosis in one artery does not predict the severity in another artery. On a group basis, however, the average severity of atherosclerosis in one artery is closely associated with the average severity in another artery*" the disease expression varies greatly among individuals and individual vascular beds (6). The clinical course is punctuated by thromboembolic events in multiple vascular beds frequently resulting in multi-organ disease (7, 8). For coronary, cerebral, peripheral, renal arterial and abdominal aortic atherosclerotic disease a coincidence ranging from 10% to 71% has been reported (9–21). However, the diagnosis of vascular multimorbidity will be critically dependent not only on the population in question but also on the methods and criteria utilized to diagnose the disease. In early studies both definition of patients' cohorts and sophistication of methods employed to diagnose the vascular disease have been deficient.

In a previous series of 423 consecutive patient admitted in 2000 for peripheral artery disease to the Department of Angiology, University Hospital Essen, vascular multimorbidity was present in 77.2% of patients (Lanzer, Rudofsky, unpublished data). Whereas it is recognized that the peripheral artery disease is an important marker of atherosclerotic multi-morbidity (22, 23), the significance of a symptomatic coronary artery disease in vascular multimorbidity appears less well understood.

Methods

Among 2034 consecutive patients admitted in 2001 to the Department of Cardiology and Angiology of the Heart Center Coswig for symptoms of coronary artery disease, a symptomatic clinically relevant coronary artery disease was documented in 1855 patients. Clinically relevant coronary artery disease was defined by the presence of angina associated with evidence for myocardial ischemia either by stress electrocardiography, stress 201thallium scintigraphy or dobutamine stress echocardiography and at least one vessel with a blockage > 50% in coronary angiography. In these patients the prevelance of a relevant non-coronary peripheral artery disease (PAD), cerebrovascular (CVD) and renal artery disease (RAD) atherosclerotic disease was determined.

Clinically relevant carotis artery disease was defined by a history of cerebrovascular events and/or presence of a greater than 40% carotis artery stenosis by PW Doppler criteria ($v_{max\ syst.} > 120$ cm/s, $v_{max\ diast.} < 40$ cm/s) (24). Carotis duplex sonography was performed in all patients with a history of cerebrovascular accidents, all patients with a high risk for an atherosclerotic disease, i.e., those with at least two main risk factors for atherosclerosis or those with a documented atherosclerotic disease in at least one non-coronary vascular bed, and in all patients scheduled for coronary artery bypass surgery. A total of 75% of all patients were screened by carotis duplex ultrasonography. In all asymptomatic patients with an internal carotid stenosis ≥80% by PW Doppler criteria and in all patients with an internal carotid stenosis ≥60% by PW Doppler criteria who were scheduled for coronary bypass surgery or those who were symptomatic, a selective bilateral cerebrovascular DSA study was subsequently performed.

Clinically relevant peripheral artery disease was defined by a history of claudication and/or ankle-brachial index (ABI) < 0.9 (25). ABI was measured in all patients studied as part of the established clinical routine. In patients with claudication and ABI < 0.9, a duplex ultrasonography of the lower leg arteries was also performed. Additional diagnostic evidence of a clinically relevant PAD was provided when at least in one artery a blockage > 50% was documented by the PW Doppler criteria (26). In patients with a history of at least Fontaine stage IIb peripheral DSA, arteriography was perfomed.

Clinically relevant renal atherosclerotic disease was considered in patients with greater than 50% renal artery stenoses on nonselective and/or selective renal cine or DSA angiography (27). Renal angiogra-

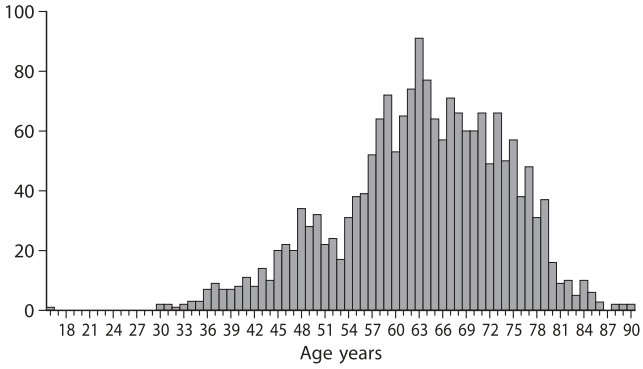

Fig. 1 Frequency distribution of ages in years (18–92 years) in all 1855 studied patients

phy was performed as a part of the coronary catherization procedure in all patients with history of hypertension requiring at least two different antihypertensive medications.

In all patients all major risk factors including type II diabetes mellitus, hypercholesterolemia, hypertension, tobacco abuse and familial history of cardiovascular disease were assessed and documented. Vascular multimorbidity was considered to be present when at least two of the assessed vascular territories had a clinically relevant disease as defined by the above stated criteria.

Statistical analysis of data on vascular multimorbidity was performed using SPSS 9.0® (SPSS Inc., Illinois, USA). To determine the dependence of vascular multimorbidity on age and sex, the patients' data has been divided into groups based on age into group A <35 years of age, group B 35–54 years of age, group C 55–74 years of age and group D ≥75 years of age and based on sex into males and females. To determine the importance of risk factors for the presence of vascular multimorbidity, a multivariate binary logistic regression was perfomed.

Results

A total of 1855 patients, mean age 65 ± 10.6 years (18–92 years), 1184 (63.8%) men and 671 (36.2%) women were studied. Age frequency distribution is shown in Figure 1. Ages <35 years old were considered low risk, patients 35–54 years old were considered moderate risk, patients 55–74 years old were considered high and those older than 75 years were considered very high risk for vascular multimorbidity. Figure 2 shows the distribution of these groups by age (Fig. 2a) and by sex (Fig. 2b and c) within the total population studied.

Among all patients studied 1265 (68.2%) patients had no evidence of noncoronary artery disease as defined in this study. In contrast, in 590 (31.8%) a significant noncoronary artery disease in at least one additional major vascular territory was documented. The most frequent combination was the association of coronary artery disease (CAD) and peripheral artery disease (PAD) disease in 176 (9.5%) patients. In 22 (1.2%) all four studied vascular territories were significantly diseased. The frequency distribution of the vascular disease of the individual vascular territories in the entire population is shown in Table 1.

Isolated coronary artery disease was present most frequently in patients younger than 35 years (87.5%) and it was the least frequent in patients older than 75 years (63.8%). The combination of coronary artery disease (CAD) with peripheral artery disease (PAD) (12.3%) and renal artery disease (RAD) (6.7%) were most frequent in patients older than 75 years, whereas the combination with cerebrovascular disease was most frequent in patients 55–74 years of age (9.4%). More complex vascular disease involving at least three major vascular territories in various combinations was observed most frequently in patients older than 75 years of age. The overall distribution of the vascular disease of the individual vascular territories by age is shown in Table 2.

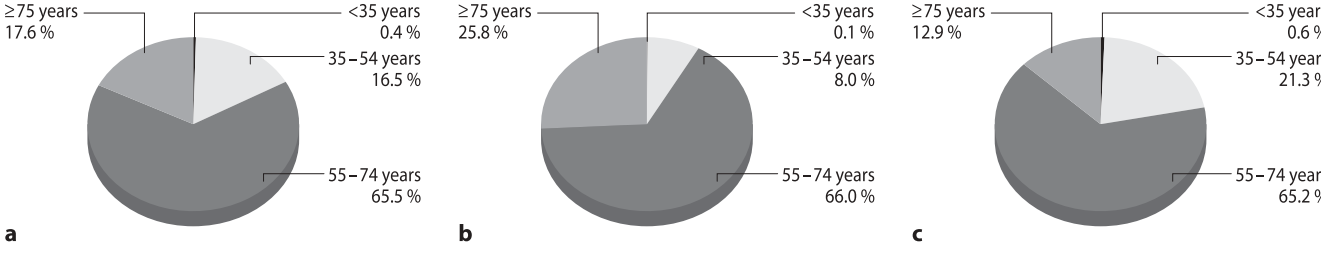

Fig. 2 Frequency distribution of patients (%) within the four age-groups in all studied patients: Group A patients <35 years (low risk category), Group B 35–54 years (moderate risk category), Group C 55–74 years (high risk category) and Group D >75 years (very high risk category) (**a**), in females (Fig. **2b**) and in males (Fig. **2c**)

Table 1 Frequency and percent distribution of patients with an isolated coronary artery disease (CAD) and patients with CAD associated with different patterns of the non-coronary vascular diseases in the studied population. *CVD* cerebrovascular disease, *PAD* peripheral artery disease, *RAD* renal artery disease

	Frequency	%
CAD	1265	68.2
CAD + CVD	160	8.6
CAD + PAD	176	9.5
CAD + CVD + PAD	91	4.9
CAD + RAD	111	6.0
CAD + CVD + RAD	12	0.6
CAD + PAD + RAD	18	1.0
CAD + CVD + PAD + RAD	22	1.2
Total	1855	100.0

The distribution of vascular disease by gender mirrored in males the distribution pattern of the entire population. In contrast, in females the highest association of CAD with peripheral artery disease (PAD((11.1%) and with renal artery disease (RAD) (13.0%) was the highest in patients 35–54 years of age as was the association of CAD, PAD and cerebrovascular disease (CVD) (5.6%). The highest incidence of CAD and CVD was observed in females 55–74 years of age (9.0%). Tables 3 and 4 show the distribution of patterns of vascular disease in males and females, respectively.

All evaluated major factors were significantly associated with the presence of vascular multimorbidity. However, when entered into a multivariant model only diabetes mellitus remained an independent risk factor and predictor of a multiterritory vascular disease (Table 5).

Discussion

Vascular diseases, and in particular atherosclerosis, are systemic disorders, typically involving multiple vascular territories (28). Thus, although the patients frequently consult a physician with symptoms related to a single organ and to its vascular bed a generalized disorder with a systemic disease and distribution of lesions is likely present. Most frequently the coronary, the cerebrovascular, renal and peripheral arteries as well as the aorta are involved.

Atherosclerosis is a lifelong disease with the first lesions occurring at an early age (29). Regardless of vascular territory the clinical manifestation usually follows a prolonged period of an asymptomatic disease. Despite of the lack of symptoms the asymptomatic stage is commonly associated with a pathologically severe and extensive disease. However, neither the planimetric extent nor the severity of the arterial wall involvement appear to predict the clinical significance of the disease reliably (30, 31). Functional parameters and more recently, inflammatory biomarkers appear more reliable prognostic indicators (32).

Symptomatic atherosclerosis is treated based on clinical symptoms secondary to the organ ischemia, whereas silent atherosclerosis may remain unrecognized and therefore untreated often for decades. Recognition of a clinically silent disease is important to step up prevention and/or in selected cases, such as findings of a severe internal carotid stenosis in coronary bypass candidates, to institute treatment.

In early studies the presence of multiterritorial vascular disease has been repeatedly reported in different populations of patients (9–21). However, due to inconsistent methods applied in these studies, particularly in regard to the definition and detection of the vascular disease, reliable data on vascular multimorbidity are scarce (33). Moreover, the importance of the major cardiovascular risk factors for the presence of a multiterritorial vascular disease has not yet been established.

In this study patients with angiographically documented clinically relevant coronary artery disease were evaluated for the presence of a co-incident disease in the peripheral, carotis and renal arteries. The presence of a non-coronary artery disease was based on clearly defined diagnostic criteria. Three major findigns of this study are recognized. First, in 31.8% of all patients with an angiographically documented clinically relevant CAD, a significant atherosclerotic disease was present in at least one additional major vascular territory. Second, type II diabetes mellitus was identified as the most important and the only independent risk factor for a multiterritory vascular disease. Third, the gender-specific patterns of vascular multimorbidity have been identified. Whereas in males vascular multimorbidity appears primarily an age dependent phenomenon occurring more frequently with an increasing age and being more frequent in all age groups when compared to females, in females vascular multimorbidity appears to depend more heavily on the presence of risk factors, specifically type II diabetes. In both sexes, coronary artery disease appears to be most frequently associated with peripheral artery disease.

Based on the increasing prevalence of the major risk factors, particularly type II diabetes worldwide (34) and due to the major demographic shifts in large populations (35) an in-depth study of vascular multimorbidity in large cohorts and in different risk populations is clearly needed. This study and the previous unpublished data (Lanzer, Rudofsky, unpublished data) suggest that in patients with documented single territory vascular disease vascular multimorbidity may be present in 31.8% to 77.2% of all patients.

Table 2 Distribution of different patterns of the multivascular disease differentiated by the disease and by the age groups within each pattern in all studied patients

	Age group				Total
	<35 years	35–54 years	55–74 years	>=75 years	
CAD					
n	7	229	821	208	1265
Disease group (%)	0.6	18.1	64.9	16.4	100.0
Age group (%)	87.5	74.8	67.6	63.8	68.2
Total (%)	0.4	12.3	44.3	11.2	68.2
CAD + CVD					
n		20	114	26	160
Disease group (%)		12.5	71.3	16.3	100.0
Age group (%)		6.5	9.4	8.0	8.6
Total (%)		1.1	6.1	1.4	8.6
CAD + PAD					
n		30	106	40	176
Disease group (%)		17.0	60.2	22.7	100.0
Age group (%)		9.8	8.7	12.3	9.5
Total (%)		1.6	5.7	2.2	9.5
CAD + CVD + PAD					
n		11	62	18	91
Disease group (%)		12.1	68.1	19.8	100.0
Age group (%)		3.6	5.1	5.5	4.9
Total (%)		0.6	3.3	1.0	4.9
CAD + RAD					
n	1	13	75	22	111
Disease group (%)	0.9	11.7	67.6	19.8	100.0
Age group (%)	12.5	4.2	6.2	6.7	6.0
'Total (%)	0.1	0.7	4.0	1.2	6.0
CAD + CVD + RAD					
n		2	7	3	12
Disease group (%)		16.7	58.3	25.0	100.0
Age group (%)		0.7	0.6	0.9	0.6
Total (%)		0.1	0.4	0.2	0.6
CAD + PAD + RAD					
n		1	13	4	18
Disease group (%)		5.6	72.2	22.2	100.0
Age group (%)		0.3	1.1	1.2	1.0
Total (%)		0.1	0.7	0.2	1.0
CAD + CVD + PAD + RAD					
n			17	5	22
Disease group (%)			77.3	22.7	100.0
Age group (%)			1.4	1.5	1.2
Total (%)			0.9	0.3	1.2
Total					
n	8	306	1215	326	1855
Disease group (%)	0.4	16.5	65.5	17.6	100.0
Age group (%)	100.0	100.0	100.0	100.0	100.0
Total (%)	0.4	16.5	65.5	17.6	100.0

Table 3 Distribution of different patterns of the multivascular disease differentiated by the disease and by the age groups within each pattern in males

	Age group				Total
	<35 years	35–54 years	55–74 years	>=75 years	
CAD					
n	6	194	517	93	810
Disease group (%)	0.7	24.0	63.8	11.5	100.0
Age group (%)	85.7	77.0	67.0	60.8	68.4
Total (%)	0.5	16.4	43.7	7.9	68.4
CAD + CVD					
n		17	74	12	103
Disease group (%)		16.5	71.8	11.7	100.0
Age group (%)		6.7	9.6	7.8	8.7
Total (%)		1.4	6.3	1.0	8.7
CAD + PAD					
n		24	72	21	117
Disease group (%)		20.5	61.5	17.9	100.0
Age group (%)		9.5	9.3	13.7	9.9
Total (%)		2.0	6.1	1.8	9.9
CAD + CVD + PAD					
n		8	48	13	69
Disease group (%)		11.6	69.6	18.8	100.0
Age group (%)		3.2	6.2	8.5	5.8
Total (%)		0.7	4.1	1.1	5.8
CAD + RAD					
n	1	6	35	7	49
Disease group (%)	2.0	12.2	71.4	14.3	100.0
Age group (%)	14.3	2.4	4.5	4.6	4.1
'Total (%)	0.1	0.5	3.0	0.6	4.1
CAD + CVD + RAD					
n		2	6	2	10
Disease group (%)		20.0	60.0	20.0	100.0
Age group (%)		0.8	0.8	1.3	0.8
Total (%)		0.2	0.5	0.2	0.8
CAD + PAD + RAD					
n		1	8	2	11
Disease group (%)		9.1	72.7	18.2	100.0
Age group (%)		0.4	1.0	1.3	0.9
Total (%)		0.1	0.7	0.2	0.9
CAD + CVD + PAD + RAD					
n			12	3	15
Disease group (%)			80.0	20.0	100.0
Age group (%)			1.6	2.0	1.3
Total (%)			1.0	0.3	1.3
Total					
n	7	252	772	153	1855
Disease group (%)	0.6	21.3	65.2	12.9	100.0
Age group (%)	100.0	100.0	100.0	100.0	100.0
Total (%)	0.6	21.3	65.2	12.9	100.0

Table 4 Distribution of different patterns of the multivascular disease differentiated by the disease and by the age groups within each pattern in females

	Age group				Total
	<35 years	35–54 years	55–74 years	>=75 years	
CAD					
n	1	35	304	115	455
Disease group (%)	0.2	7.7	66.8	25.3	100.0
Age group (%)	100.0	64.8	68.6	66.5	67.8
Total (%)	0.1	5.2	45.3	17.1	67.8
CAD + CVD					
n		3	40	14	57
Disease group (%)		5.3	70.2	24.6	100.0
Age group (%)		5.6	9.0	8.1	8.5
Total (%)		0.4	6.0	2.1	8.5
CAD + PAD					
n		6	34	19	59
Disease group (%)		10.2	57.6	32.2	100.0
Age group (%)		11.1	7.7	11.0	8.8
Total (%)		0.9	5.1	2.8	8.8
CAD + CVD + PAD					
n		3	14	5	22
Disease group (%)		13.6	63.6	22.7	100.0
Age group (%)		5.6	3.2	2.9	3.3
Total (%)		0.4	2.1	0.7	3.3
CAD + RAD					
n		7	40	15	62
Disease group (%)		11.3	64.5	24.2	100.0
Age group (%)		13.0	9.0	8.7	9.2
'Total (%)		1.0	6.0	2.2	9.2
CAD + CVD + RAD					
n			1	1	2
Disease group (%)			50.0	50.0	100.0
Age group (%)			0.2	0.6	0.3
Total (%)			0.1	0.1	0.3
CAD + PAD + RAD					
n			5	2	7
Disease group (%)			71.4	28.6	100.0
Age group (%)			1.1	1.2	1.0
Total (%)			0.7	0.3	1.0
CAD + CVD + PAD + RAD					
n			5	2	7
Disease group (%)			71.4	28.6	100.0
Age group (%)			1.1	1.2	1.0
Total (%)			0.7	0.3	1.0
Total					
n	1	54	443	173	671
Disease group (%)	0.1	8.0	66.0	25.8	100.0
Age group (%)	100.0	100.0	100.0	100.0	100.0
Total (%)	0.1	8.0	66.0	25.8	100.0

Table 5 Frequency distribution of the five major cardiovascular risk factors type II diabetes, hypercholesterolemia, cigarette smoking, hypertension and familiar predisposition in patients with an isolated CAD [vascular morbidity 1 (CAD)] and in patients with CAD associated with different patterns of the non-coronary vascular disease [vascular morbidity > 1]

		Vascular Morbidity		Total
		1 (CAD)	> 1	
Diabetes				
No	n	839	333	1172
	Diabetes (%)	71.6	28.4	100.0
	Vascular Multimorbidity (%)	66.3	56.4	63.2
	Total (%)	45.2	18.0	63.2
Yes	n	426	257	683
	Diabetes (%)	62.4	37.6	100.0
	Vascular Multimorbidity (%)	33.7	43.6	36.8
	Total (%)	23.0	13.9	36.8
Total	n	1265	590	1855
	Diabetes (%)	68.2	31.8	100.0
	Vascular Multimorbidity (%)	100.0	100.0	100.0
	Total (%)	68.2	31.8	100.0

		Vascular Morbidity		Total
		1 (CAD)	> 1	
Cholesterolemia				
No	n	686	349	1035
	Cholesterolemia (%)	66.3	33.7	100.0
	Vascular Multimorbidity (%)	54.2	59.2	55.8
	Total (%)	37.0	18.8	55.8
Yes	n	579	241	820
	Cholesterolemia (%)	70.6	29.4	100.0
	Vascular Multimorbidity (%)	45.8	40.8	44.2
	Total (%)	31.2	13.0	44.2
Total	n	1265	590	1855
	Cholesterolemia (%)	68.2	31.8	100.0
	Vascular Multimorbidity (%)	100.0	100.0	100.0
	Total (%)	68.2	31.8	100.0

		Vascular Morbidity		Total
		1 (CAD)	> 1	
Nicotin				
No	n	1053	486	1539
	Nicotin (%)	68.4	31.6	100.0
	Vascular Multimorbidity (%)	83.2	82.4	83.0
	Total (%)	56.8	26.2	83.0
Yes	n	212	104	316
	Nicotin (%)	67.1	32.9	100.0
	Vascular Multimorbidity (%)	16.8	17.6	17.0
	Total (%)	11.4	5.6	17.0
Total	n	1265	590	1855
	Nicotin (%)	68.2	31.8	100.0
	Vascular Multimorbidity (%)	100.0	100.0	100.0
	Total (%)	68.2	31.8	100.0

		Vascular Morbidity		Total
		1 (CAD)	> 1	
Hypertension				
No	n	317	134	451
	Hypertension (%)	70.3	29.7	100.0
	Vascular Multimorbidity (%)	25.1	22.7	24.3
	Total (%)	17.1	7.2	24.3
Yes	n	948	456	1404
	Hypertension (%)	67.5	32.5	100.0
	Vascular Multimorbidity (%)	74.9	77.3	75.7
	Total (%)	51.1	24.6	75.7
Total	n	1265	590	1855
	Hypertension (%)	68.2	31.8	100.0
	Vascular Multimorbidity (%)	100.0	100.0	100.0
	Total (%)	68.2	31.8	100.0

		Vascular Morbidity		Total
		1 (CAD)	> 1	
Genetic Predosposition				
No	n	1159	546	1705
	Gen Predisp (%)	68.0	32.0	100.0
	Vascular Multimorbidity (%)	91.6	92.5	91.9
	Total (%)	62.5	29.4	91.9
Yes	n	106	44	150
	Gen Predisp (%)	70.7	29.3	100.0
	Vascular Multimorbidity (%)	8.4	7.5	8.1
	Total (%)	5.7	2.4	8.1
Total	n	1265	590	1855
	Gen Predisp (%)	68.2	31.8	100.0
	Vascular Multimorbidity (%)	100.0	100.0	100.0
	Total (%)	68.2	31.8	100.0

The major limitation of this study represents the incomplete screening for the presence of a clinically relevant cerebrovascular disease (75% of all patients) and for the presence of a hemodynamically significant renovascular disease (only patients with poorly controlled hypertension requiring at least two different medications recieved renal arteriography). Incomplete screenig is likely to underestimate the true prevalence of the atherosclerotic disease in these two locations in this study. Furthermore, the small sample size in the individual subgroups has limited the statistical power, particularly in patients younger than 35 years of age and in those subgroups with less frequent combinations of vascular involvement such as CAD associated RAD. In addition, a bias due to the high regional prevalence of vascular diseases in Saxony-Anhalt (36) and other referral pattern related factors can not be excluded in this study. Finally, the impact of the newer cardiovascular risk factors on the presence of multiterritory vascular disease has not been elucidated (37).

Table 6 A multivariate binary logistic regression of the major cardiovascular risk factors type II diabetes, hypercholesterolemia, cigarette smoking, hypertension and familiar predisposition associated with a multiterritory vascular disease

Risk factor	Estimator	Significance (p)	Risk (OR)
Diabetes	0.4036	0.001	1.4972
Smoking	0.1340	0.3191	1.1433
Hypertension	0.1139	0.3401	1.1206
Dyslipoproteinemias	–0.1783	0.0813	0.8367
Genetic Predosposition	–0.1738	0.3583	0.8405

However, based on the results of this study and based on previous observations multiterritory vascular disease represents a new potentially important clinical aspect of the medical management of patients with coronary artery disease and clearly deserves further in-depth elucidation.

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References

1. McGill H Jr (ed) (1968) The geographic pathology of atherosclerosis. Lab Invest 18:465–639
2. Atherosclerosis of the aorta and coronary arteries in five towns (1976) Bulletin World Health Organization. Geneve, pp 485–638
3. Asakura M, Ueda Y, Yamaguchi O et al (2001) Extensive development of vulnerable plaques as a pan-coronary process in patients with myocardial infarction: an angioscopic study. J Am Coll Cardiol 37:1284–1288
4. Goldstein JA, Demetrious D, Grines C et al (2000) Multiple complex coronary plaques in patients with acute myocardial infarction N Engl J Med 343:915–922
5. Vita J (2002) Clinical assessment of endothelial function. In: Lanzer P, Topol EJ (ed) PanVascular Medicine: Integrated Clinical Management. Springer Verlag, Berlin Heidelberg New York, pp 691–700
6. McGill HC Jr, Arias-Stella J, Carbonell LM et al (1968) General findings of the International Atherosclerosis Project. Lab Invest 18:498–502
7. Aronow WS, Ahn C (1994) Prevalence of coexistence of coronary artery disease, peripheral arterial disease, and atherothrombotic brain infarction in man and women >62 years of age. Am J Cardiol 74:64–65
8. Cooper R, Cutler J, Desvigne-Nickens P et al (2000) Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States. Findings of the National Conference on Cardiovascular Disease Prevention. Circulation 102: 3137–3147
9. Cirillo F, Renzulli A, Leonardo G et al (2001) Associated vascular lesions in patients undergoing coronary artery bypass grafting. Acta Cardiol 56:91–96
10. Atmer B, Jogestrand T, Laska J, Lund F (1995) Peripheral artery disease in patients with coronary artery disease. Int Angiol 14:89–93
11. Wilt TJ, Davies BR, Meyers DG et al (1996) Prevalence and correlates of symptomatic peripheral atherosclerosis in individuals with coronary heart disease and cholesterol levels less than 240 mg/dL: baseline results from the Cholesterol and Recurrent Events (CARE) Study. Angiology 47:533–541
12. Atmer B, Jogestrand T, Laska J, Lund F (1995) Peripheral artery disease in patients with coronary artery disease. Int Angiol 14:89–93
13. Harding MB, Smith LR, Himmelstein SI et al (1992) Renal artery stenosis: prevalence and associated risk factors in patients undergoing routine cardiac catheterization. J Am Soc Enthral 2:1608–1616
14. Hertzer NR, Beven EG, Young JR et al (1984) Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. Ann Surg 199:223–233
15. Valentine RJ, Grayburn PA, Eichborn EJ et al (1994) Coronary artery disease is highly prevalent among patients with premature peripheral vascular disease. J Vasc Surg 19:668–674
16. Simons PC, Algra A, Eikelboom BC et al (1999) Carotid artery stenosis in patients with peripheral arterial disease: the SMART study. SMART study group. J Vasc Surg 30:519–525
17. Cheng SW, Wu LL, Ting AC, Wong J (1999) Prevalence of significant carotid stenosis in Chinese patients with peripheral and coronary artery disease. Aust N Z J Surg 69:44–47
18. Alexandrova NA, Gibson WC, Norris JW, Maggisano R (1996) Carotid artery stenosis in peripheral vascular disease. J Vasc Surg 23:645–649
19. Herzter NR, Young JR, Beven EG et al (1985) Coronary angiography in 506 patients with extracranial cerebrovascular disease. Arch Intern Med 145:849–852
20. Allan PK, Mowbray PI, Lee AJ, Fowkes FG (1997) Relationship between carotid intima-media thickness and symptomatic and asymptomatic peripheral arterial disease. The Edinburgh Artery Study. Stroke 28:348–353
21. Young JR, Herzter NR, Beven EG et al (1986) Coronary artery disease in patients with aortic aneurysm: a classification of 302 coronary angiograms and results of surgical management. Ann Vasc Surg 1:36–42
22. Criqui MH, Langer RD, Fronek A et al (1992) Mortality over a period of 10 years in patients peripheral arterial disease. N Engl J Med 326:381–386
23. Newman AB, Shemanski L, Manolio TA et al (1999) Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. The Cardiovascular Health Study Group. Arterioscler Thromb Vasc Biol 19:538–545
24. Meairs S, Hennerici M (2002) Cerebrovascular ultrasonography. In: Lanzer P, Topol EJ (eds) PanVascular Medicine, Integrated Clinical Approach. Springer, Berlin, pp 420–440
25. Newmann AB, Siscovick DS, Manolio TA et al (1993) Ankle-arm index as a marker of atherosclerosis in the Cardiovavascular Health Study. Circulation 88:837–845
26. Jäger KA, Rickets HJ, Strandness DE Jr (1985) Duplex scanning for evaluation of lower limb arterial disease. In: Bernstein EF (ed) Noninvasive diagnostic techniques in vascular disease. Mosby, St Louis, pp 619–631

27. Schoenberg SO, Bock M, Kallinowski F et al (2000) Correlation of hemodynamic impact and morphologic degree of renal artery stenosis in a canine model. J Am Soc Nephrol 11:2190–2198
28. Bates SR, Gangloff ED (eds) (1985) Atherogenesis and aging, Springer, New York
29. Stary HC (1989) Evolution and progression of atherosclerotic lesions in coronary arteries of children and young adults. Atherosclerosis (Suppl I)I-9–I-19
30. Daoud AS, RA Florentin, F Goodale (1964) Diffuse coronary atherosclerosis versus isolated plaques in the etiology of myocardial infarction. Am J Cardiol 32:69–74
31. Little WC, Constantinescu M, Applegate RJ, Kutcher MA, Burrows MT, Kahl FR, Santamore WP (1988) Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? Circulation 78:1157–1166
32. Ridker PM, Rifal N, Rose L et al (2002) Comparison of C-reactive protein and low-density lipoprotein cholesterol level inn the prediction of first cardiovascular event. N Engl J Med 347:1557–1565
33. CAPRIE Steering Committee (1996) A randomized, blinded, trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE). Lancet 348:1329–1339
34. Zimmet P, Alberti KGMM, Shaw J (2001) Global and societal implications of the diabetic epidemic. Nature 414:782–787
35. http://esa.un.org/unpp/p2k0data.asp
36. Willich SN, Löwel H, Mey W, Trautner C (1999) Regionale Unterschiede der Herz-Kreislauf Mortalität in Deutschland. Deutsches Ärtzebl 96:A-483–A-488
37. O'Donell CJ, Kannel WB (2002) Epidemiology of atherosclerotic vascular disease. In: Lanzer P, Topol EJ (eds) PanVascular Medicine. Springer, pp 3–16

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Core Curriculum

Expanding the Base for Teaching of Percutaneous Coronary Interventions: The Explicit Approach

Peter Lanzer,[1] MD and Lutz Prechelt,[2*] PhD

Objectives: Accelerate and improve the training and learning process of operators performing percutaneous coronary interventions (PCI). Background: Operator cognitive, in particular decision-making skills and technical skills are a major factor for the success of coronary interventions. Currently, cognitive skills are commonly developed by three methods: (1) Cognitive learning of rules for which statistical evidence is available. This is very incomprehensive and isolates cognitive learning from skill acquisition. (2) Informal tutoring received from experienced operators, and (3) personal experience by trial-and-error are both very slow. Methods: We propose in this concept article a conceptual framework to elicit, capture, and transfer expert PCI skills to complement the current approach. This includes the development of an in-depth understanding of the nature of PCI skills, terminology, and nomenclature needed to streamline communication, propensity of reproducible performance assessment, and in particular an explication of intervention planning and intra-intervention decision-making. We illustrate the impact of improved decision-making by simulation results based on a stochastic model of intervention risk. Results: We identify several key concepts that form the basis of this conceptual framework, in particular different risk types and the notions of strategy, interventional module, and tactic. Conclusions: The increasing complexity of cases have brought PCI to the point where the decision-making skills of master operators need to be made explicit to make them systematically learnable such that the skills of beginner and intermediate operators can be improved much faster than is currently possible. © 2010 Wiley-Liss, Inc.

Key words: percutaneous coronary interventions; learning; training; teaching; knowledge explication

INTRODUCTION

Percutaneous coronary intervention (PCI) is a highly complex activity requiring many cognitive and technical skills based on highly specialized knowledge. Traditionally, the trainee learns these skills mainly by observing and imitating his mentor. With growing experience, the trainee begins to perform his own supervised cases, proceeding from simple to more complex interventions. Eventually, the trainee acquires sufficient skills to work independently and to develop his own clinical expertise. This approach, which we call the empirical approach, is primarily based on tacit transfer of knowledge relying on the internalization of a mentor's skills and to a lesser degree on verbal instructions or written documentation. Although the empirical approach represents a powerful teaching strategy, it has several important shortcomings. First, it is highly dependent on the availability of highly qualified mentors. Second, it is highly dependent on the ability of trainees to grasp and to assimilate essential skills implicit in the mentor's performance. Third, lacking consistent externalization and codification of the mentors' skills, the state of practice is subject to considerable

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TABLE I. Components of Explicit Teaching of PCI Skills

Definition and analysis of the formal structure of the PCI process
Development and updating of standardized terminology
Definition, analysis, and acquisition of the essential cognitive and motor procedure-related skills
Definition, analysis, and development of the decision making process
Structuring and staging of the teaching process

TABLE II. Basic Pattern of PCI

Initialization
Main interventional cycle (MIC)
Termination
Aftercare
Follow-up

TABLE III. Essential Components of PCI Strategy Design

Analysis of the patient-related factors, e.g., in PCI: comorbidities, especially diabetes, status of the global and regional left ventricular function, status of the renal function, etc.
Analysis of the target-lesion-related factors, e.g., in PCI: angiographic morphology including the proximal and adjacent segments, number and topographic distribution of concomitant lesions, etc.
Comprehensive risk assessment
Definition of the aim of the intervention
Planning of MIC as a sequence of interventional modules (IMs)

fluctuations between individuals and institutions leading to "substantial variation in the quality of PCI services" [1]. Fourth, the low degree of reproducibility and standardization makes advances in the state of the art difficult. To improve the transfer of cognitive PCI skills, we propose to expand the base for teaching by an explicit approach based on the externalization, codification, and systematization of PCI skills by the interventional community.

Introduction to Explicit Teaching

Fundamentally, knowledge and cognitive skills can be transferred and acquired tacitly using nonverbal means of communication or explicitly using verbal instructions. Whereas the tacit mode relies primarily on somatic experiences and subsidiary awareness associated with conceptual activities, the explicit mode depends on focal awareness, externalization, and verbal communication of knowledge [2]. In advanced teaching, both approaches are complementary. In this article, we shall not address the technical skills and focus on the cognitive skills instead, in particular on decision-making. The fundamental assumption underlying this work states that sound decision-making can be learned by mastering a coherent set of patterns and that these patterns can be presented based on a modest number of basic concepts that together describe a formal structure of the interventional process. It is these basic concepts that the present article is concerned with. Table I provides a first overview.

Formal Structure of Percutaneous Coronary Interventions

All percutaneous coronary interventions exhibit a single formal structure, a linear sequence of five distinct phases as shown in Table II. The first three phases represent PCI proper.

Initialization comprises all preparatory steps up to the placement of the guiding catheter at the ostium of the target vessel and acquisition of the first preinterventional angiogram. In all interventions the crucial step is the design of a specific case-related strategy based on findings and clinical presentations. Essential components of PCI strategy design are summarized in Table III.

Assessment of patient- and lesion-related factors is critical for risk assessment and definition of suitable aims for the intervention. At the heart of strategy formation is a suitable plan for the main interventional cycle, MIC: What steps will be done in what order, what will each of them achieve, when will the procedure be terminated? An appropriate selection of the steps and a sufficiently accurate expectation for their impact are key contributors to a quality intervention. Constituents steps of the strategy are interventional modules, IM (see section Strategies).

MIC represents the core of a PCI. Ideally, it follows the designed strategy and consists of a foreseen number of rounds. Each round (except the last one) consists of two basic phases:

1. Angiographic image acquisition, evaluation, and decision upon action.
2. Performing the action, which can be either an interventional or a diagnostic step.

The decision in round N is always based on the outcome of the previous round $N - 1$. The minimum number of rounds is $N = 2$, e.g., direct stenting; complex interventions may consist of up to $N = 50$ rounds, rarely more. Each round is designed to advance the intervention toward the stated goal. The last round lacks an action and triggers the termination. In general, the number of rounds comprising a MIC should be kept at a minimum, as the total risk of the intervention increases with each round. IMs are generic mental representations of rounds constituting a specific MIC (see later).

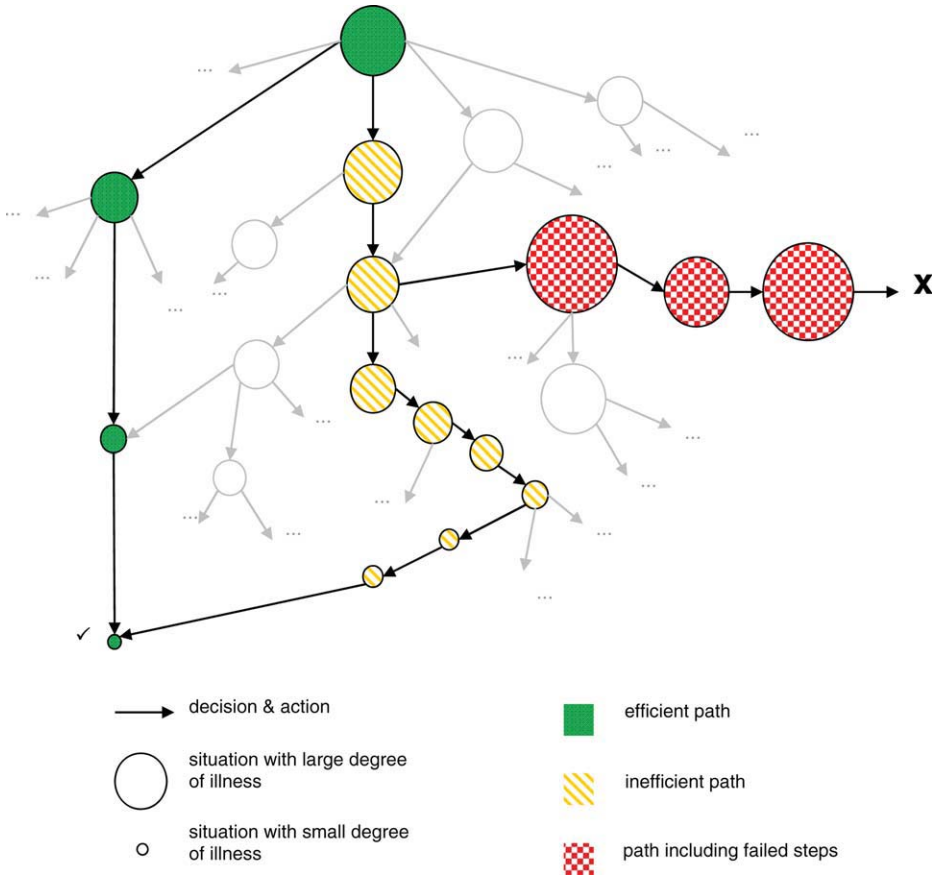

Fig. 1. Importance of decision-making in PCI: Good decisions lead to fast progress (left), sub-optimal decisions lead to slower progress (middle), bad decisions can be counter-productive (right) and may lead to failed interventions (X). There are millions of possible paths through the decision space of even modestly complex interventions.

Termination concludes the intervention proper starting with the removal of the instrumentation and ending with the closure of the access site. Aftercare spans the entire hospital stay following the intervention. Follow-up refers to the time following the discharge; typical time-frames are 30-days, 6 months, and 1 year after the index intervention.

Essential Cognitive Skills

Essential cognitive skills are interrelated and specific to the various phases that can be distinguished in PCI. For example, reading and interpreting coronary angiograms throughout the course of the PCI represents one of the basic cognitive skills required for PCI mastery. These skills are in turn embedded in a more complex category of skills responsible for the overall monitoring of the evolution of the intervention. These specific and more complex cognitive skills can be summarized in compound skills such as focused attention, i.e., the ability to screen out distracting stimuli, sustained attention, i.e., the ability to maintain vigilance, divided attention, i.e., the capability to recognize and respond to multiple stimuli at the same time, alternating attention, i.e., the ability to shift the focus of attention quickly, central processing speed, i.e., the time it takes to encode, categorize, and understand the meaning of any sensory stimuli, conceptual reasoning including concept formation, abstraction, deductive and inductive logic, working memory, i.e., the ability to hold enough task-relevant information while processing it, response inhibition, i.e., the ability to avoid reflexively reacting to incorrect stimuli, visual processing speed, i.e., the time it takes to analyze visual stimuli, visual scanning and tracking, i.e., the ability to find and follow a visual cue, visuo-spatial classification, i.e., the ability to discriminate between visual objects based on a concept or rule, etc. Cognitive skills are fundamental to all decision making in PCI and they can be trained.

Decision-Making

Decision-making (DM) occurs in strategy formation and in each round of the MIC in real-life interventions.

It represents the most critical determinant of the PCI outcome. Although the number of possible actions in each round is limited, the combined effects of multiple rounds create a huge decision space with a high degree of uncertainty (Fig. 1).

To date DM in PCI has not yet been sufficiently studied likely because it was perceived too complex to allow a meaningful characterization. Yet, DM in PCI is similar to other probabilistic DM processes associated with complex cognitive activities [3], such as OPCAB surgery [4]. To develop PCI teaching programs based on the explicit training of the cognitive skills, the critical formative importance of some basic concepts outlined below must be appreciated.

Risk. Qualitatively, risk represents the possibility of a specific adverse outcome in a given patient. Quantitatively, risk is defined as the probability of a specific adverse outcome multiplied by the magnitude of the expected damage. Exact quantification of either of these parameters is usually infeasible, but the principles of fuzzy sets [5] or probability range qualifiers such as very high ($>10\%$), high ($\geq 3\%$), moderately high ($<3\%$), low ($<1\%$), and very low ($<0.1\%$) can be helpful to describe the risk of specific complications in PCI.

Fundamentally we have to discriminate the risk inherent in the patient's health status, which we call latent risk (e.g., the risk of heart failure following myocardial infarction), from the risk incurred by the intervention itself, which we call actional risk (e.g., the damage of the target vessel due to a balloon inflation). Reductions in latent risk are a way of expressing the benefits obtained for the patient and short-term and long-term benefits should be considered in a balanced manner. For instance, long-term considerations may in some cases speak against using a stent, since the presence of a stent could make a possibly needed future intervention or surgery more difficult. Actional risk can be divided into several parts. The following are the most important ones: Optimum-skill actional risk is the risk of damage to the patient even if the chosen intervention is performed with perfect skill by an ideal interventionist. This risk is never zero and it is thus unavoidable. Knowledge risk is the actional risk due to incomplete information about the status of the target lesion and status of the patient (e.g., thrombotic lesion not visualized by angiography). This risk may be small, but will never be zero. Skill risk reflects the fact that real interventionists are not ideal and will hence not perform the step in a perfect manner. It may be small when the interventionist is very skilled or larger if not [6].

Based on this risk concept, the following rules would apply to decision-making in PCI:

1. At each step during an intervention, the total risk should be minimized; thus all plausible actions should be considered, the actional risk incurred and the latent risk saved by each assessed and those steps with the least sum of both should be selected.
2. As long as the intervention produces overall benefits for the patient, the total risk will become smaller in each step, except for sudden changes in latent risk, e.g., due to patient instability.
3. To minimize the total actional risk the number of rounds should be kept at a minimum; rounds reducing the risk of subsequent rounds must be evaluated in light of their own actional risk.
4. To prevent escalations in procedures with increasing risk, termination of the intervention, or other treatment options should be considered.

To apply the above risk-based decision-making framework perfectly, the extremely difficult task of risk quantification would need to be approached. Systematic evaluation of risk and feed-back on adverse events shall improve operators' ability to judge the risk properly.

Strategies. As introduced above, a strategy (or "interventional strategy" in full) is a complete plan of an intervention. Thus, a strategy represents the expectation about the most likely course the intervention will take as a whole. This expectation is based on the interventionist's experience about sequences of actions that are useful and consequences that are likely. Strategies are the critical constituent of initialization because they postulate how to achieve the best possible outcome at minimum risk. Although strategies are case-specific they employ sequences of premeditated and semi-standardized steps we call interventional modules (IMs). IMs are generic mental representations of MIC rounds in real-life interventions. An IM is selected from a library of IMs based on patient and lesion characteristics and the interventionist's experience. They describe intermediate situations that are common during interventions, the specific decisions and corresponding rationale, the respective action to be taken, and the outcome that is both expected (i.e., likely) and intended (i.e., positive progress of the intervention). As such they are the natural building blocks of interventional strategies [7].

Safe navigation of the huge decision space associated with PCI is guided by observation of the accepted interventional rules i.e., definite and usually mandatory standards of conduct and interventional recommendations i.e., less strict suggested standards of conduct such as guidelines. However, although the interventional rules and recommendations at present regulate the overall PCI process they cut off only a few small

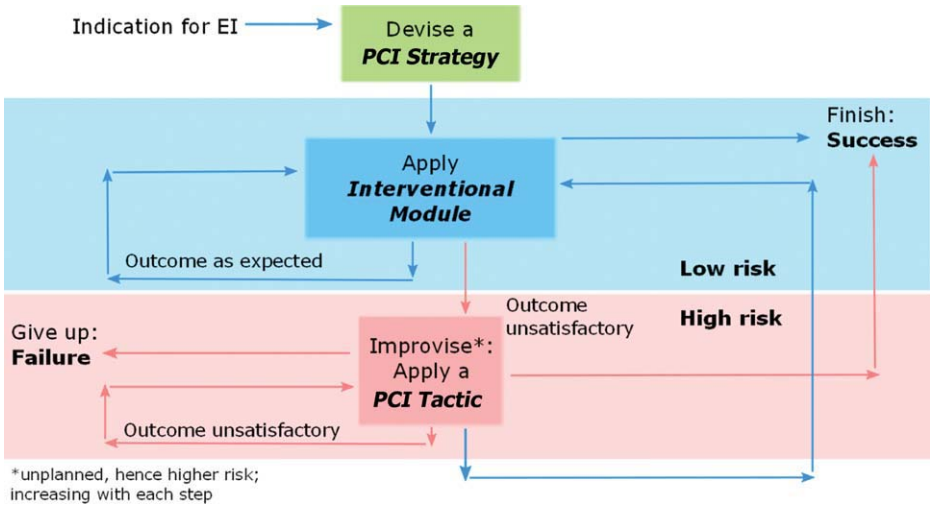

Fig. 2. Summary of strategy alone and combined strategy and tactics driven PCI. In principle, both, strategy-based and mixed strategy-based and improvisation-driven PCI may result in success or failure. However, the probability of success is higher and the level of risk is lower in strategy based (blue panel) compared to mixed strategy-based and improvisation-driven PCI.

corners of the actual total PCI decision space; most of it has to be navigated based on the applied skills of the individual interventionist.

The quality of strategies can be determined by comparing outcomes of actual interventions conducted in similar clinical scenarios. Master strategies allow reasonably accurate predictions regarding the likely outcome, the amount of total risk at each point, and the utilization of resources such as time and material. They also allow preparing in advance for emergencies and complications by implementing preventive measures. However, perhaps the most important benefit of the consequent implementation of strategies is development and establishment of stable interventional routines. Routine intervention means the embodiment of series of interventional actions within a given clinical context correctly predicted by individual interventional strategies of one particular interventionist. Routine interventions allow a smooth and successful conduct of entire procedures at predictable and low risk. Routine interventions are therefore safe, effective, and efficient. They enable the interventionist to fully focus on the evolving procedure and are the basis for successful treatment of increasingly complex cases over time.

Tactics. An ideal intervention will follow the designed strategy step-by-step. However, in the real world of clinical practice, even the conduct of a master strategy will sometimes produce unexpected outcomes forcing the interventionist to deviate from the plan and to perform unplanned interventional actions. Changes of strategies enforced by the unpredicted results of interventional actions in real procedures we call tactics and their constituent rounds we call impromptu actions, IAs. Minor deviations from strategies include insertions of single IAs; more substantial changes require introduction of a series of IAs or switching to a different strategy; extreme cases may require more or less complete deviation from the preconceived strategy or even premature termination. Like strategies, interventional tactic are specific to a patient and situation. In contrast to strategies, interventional tactic often have to be chosen under severe time constrains and require therefore even higher clinical judgment skills. The ability to make the right decision and to perform the right actions at the right time under pressure and frequently in emergency situations is a hallmark of master interventionists. In these instances, the interventional decisions appear to be instructed by intuition, a state of mind of highly trained professionals likely rooted in embodiment of a broad spectrum of interventional routines and expressed in abilities to conceptualize and to handle non- routine events instantaneously. Nevertheless, regardless of the skill level of individual interventionists it appears that routine interventions carry a lower procedural risk compared to tactic-guided interventions [8]. Figure 2 summarizes the interplay between predesigned strategy and tactics.

Illustrative examples. To illustrate the impact of forming sound or ill-suited strategies and of making correct or shaky tactical judgments, we designed a simple stochastic simulation model as follows:

- The initial strategy expects that the intervention will take N rounds (here: $N = 4$ rounds for a simple case, $N = 10$ rounds for a complicated one).

- An intervention will be stopped because of the excessive risks as soon as it becomes clear that it cannot be finished in 40 rounds or less.
- In any round i, the result will be different from the expected result in D percent of the cases (we assume $D = 10$ for a master operator, $D = 15$ for an intermediate, and $D = 30$ for an inexperienced one). When this happens, it will often make one or two additional rounds necessary or, occasionally, save one round.
- However, in B percent of the rounds, the unexpected result was actually the consequence of a rather bad judgment and the effects are much more negative: two to four additional rounds become necessary. We assume that $B = 2$ for a master operator, $B = 10$ for an intermediate, and $B = 20$ for an inexperienced one.
- The number C_i of plausible action choices to be considered in round i fluctuates, with a mean of 3. However, after a bad judgment with negative effects, C_i is twice as large as usual.
- The decision space grows exponentially as the process unfolds; in each step, its size multiplies by C_i.

Using this model for a number of stochastic simulations, Fig. 3 provides examples of the evolution and outcome of some standard interventions, three each conducted by a master, intermediate, and inexperienced interventionist, respectively.

Using the same format, Fig. 4 shows the evolution and outcome of complex interventions. These simulations allow for the following observations:

- Standard interventions do sometimes and complicated ones do usually take longer than initially expected. The better the judgment capabilities of the operator, the smaller is the difference.
- With low judgment capabilities, complex interventions may escalate, i.e., in their course, the remaining work to be done gets more rather than less and the risk increases. With increasing judgment capabilities, strength, and frequency of such crises decrease gradually.

Although this model is far too simplistic for making quantitative predictions of actual interventions, it clearly demonstrates the consequences of less-than-ideal strategic planning and tactical judgment and emphasizes the need to train both.

Terminology and nomenclature. The ability to capture, elicit, articulate, and transfer expert cognitive skills a comprehensive, precise, and standardized terminology is required. Although in PCI an extensive terminology has already been developed [9–11] most of the available terms relate to conditions before, during, or after interventions; terminology referring directly to the cognition and actual performance is scarce. Thus, development of operational terminology enabling differentiations between the individual aspects of the ongoing DM and IAs appears indispensable to allow systematic step-by-step tracking, verbalization of the relevant decision points and individual actions, and consistent feed-back and evaluation. The accepted terms should be properly substantiated and standardized. For example, current clinical jargon commonly uses the terms pushability, crossability, and trackability, but these refer quite loosely to a whole range of different phenomena; instead, they should be clearly defined [12].

Knowledge- and Cognitive Skill-Based Curriculum

Formal structure and objectives of training curricula in interventional cardiology have been defined both in Europe and in the USA [1,13–16]. These documents state and set standards for training. However, although the scope of training is clearly outlined, little space is devoted to learning techniques and actual skill acquisition. In the daily practice of most PCI fellowship programs, some elements of explicit cognitive teaching are likely present, however a comprehensive and standardized foundation is as of yet lacking.

To develop a consistent way of cognitive skill acquisition we suggest in this concept article the development of a library of interventional cases and teaching regimes.

Library of interventional real-life cases. The library of real-life PCI cases will provide a representation of the entire spectrum of coronary interventions in typical scenarios, e.g., left main, left main ostium, stem or bifurcation in elective and emergency settings. The cases are documented in a standard format, e.g., image definition of the target vessel in moderate magnification in two best projections, definition of the target site in high magnification in two orthogonal projections, definition of all relevant decision points, definition of the final results in high magnification in two orthogonal projections, definition of the target vessel in moderate magnification in two best projections. The image documentation is completed by a written procedural report including instrumentation and brief commentary of the operator on decision points.

Meaningful case analysis requires a handful of experts willing to agree on criteria to assess the quality and merits of individual PCIs. Analysis of a sufficient number of properly categorized representative cases, constitute the library of interventional knowledge allowing case selection and stratification in standard, intermediate, and complex categories. Classes of cases

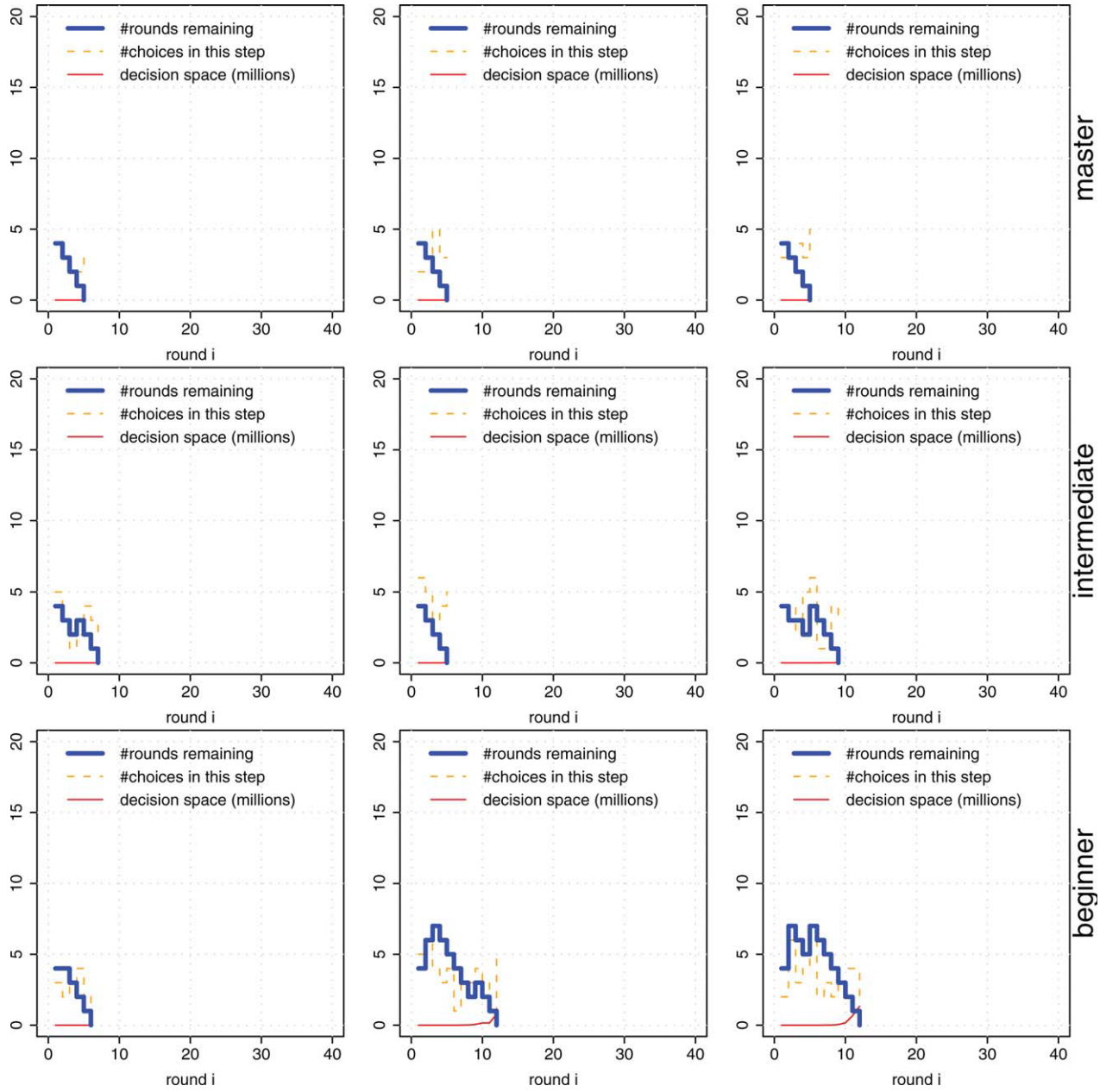

Fig. 3. Stochastic simulation of the course of nine different random standard interventions (*N* = 4 rounds expected duration) for a master operator (top row), an intermediate operator (middle row), and an inexperienced beginning operator (bottom row). All three master interventions go just as planned; two of the intermediate interventions need a few additional steps; two of the beginner's interventions initially even make matters worse and eventually take much longer than required.

documented and analyzed in a standardized and reproducible fashion serve as teaching materials in individual program settings. They assist the learner with interpreting, reasoning, and decision making activities that comprise the routine and nonroutine tasks allowing for corrective feedback and structured development of task specific cognitive skills and ultimately declarative knowledge [17].

Teaching regime. Our knowledge- and cognitive skill-based concept will complement the currently prevalent mostly tacit teaching of cognitive skills it in three basic stages of learning.

The first stage involves the classical learning "from the books." Here the trainee acquires the basic knowledge about PCI according to the tenets outlined in the current curricula on clinical competence in

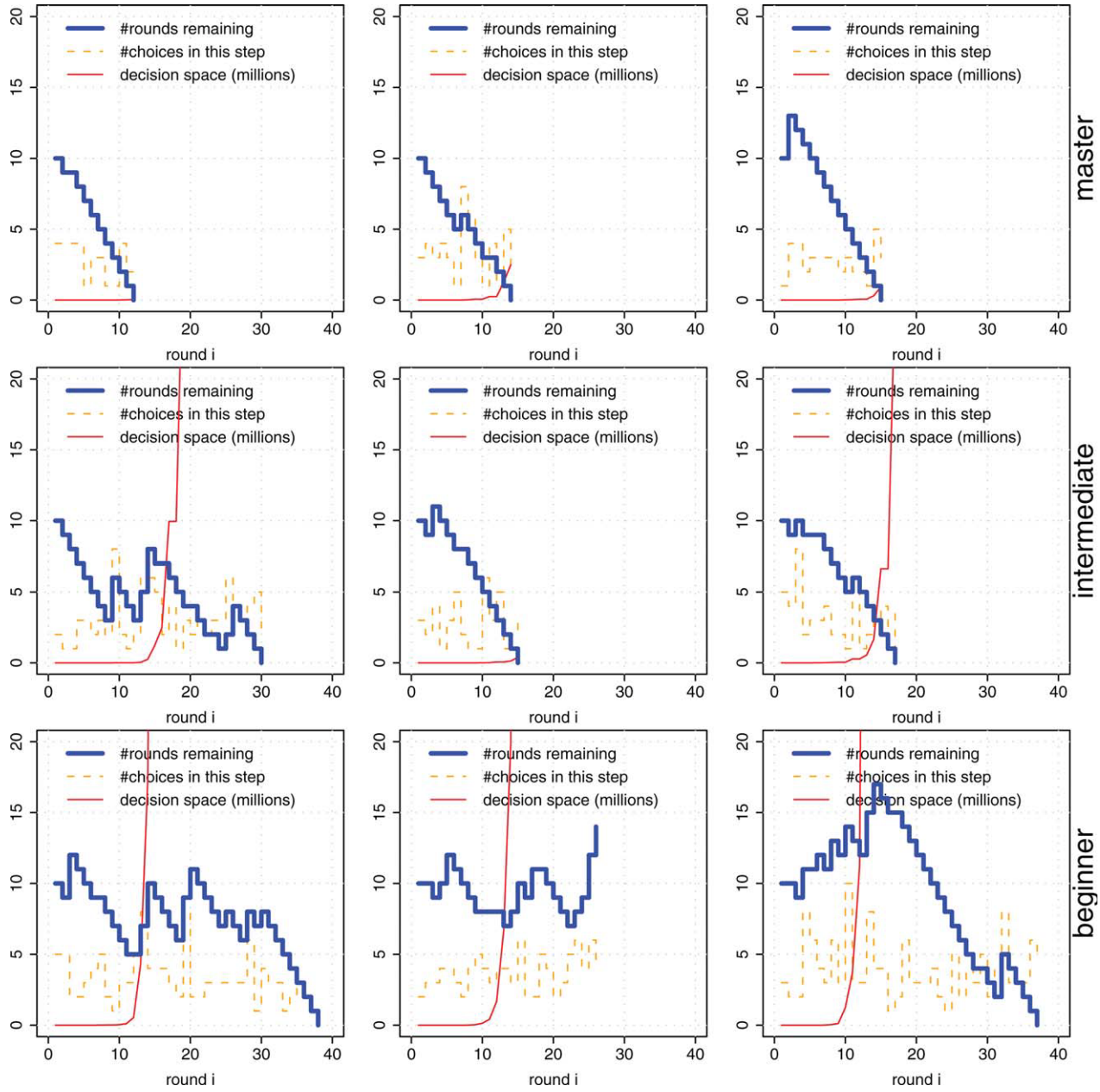

Fig. 4. Stochastic simulation of the course of nine different random complex interventions (*N* = 10 rounds expected duration) for a master operator (top row), an intermediate operator (middle row), and an inexperienced beginning operator (bottom row). Not one of the nine interventions goes exactly as planned and none of the operators can always avoid making matters initially worse. However, the master operator can finish all of his interventions in 11–14 steps; the intermediate can sometimes finish almost as fast (14 and 16 steps), but encounters one case where the intervention steers far off course, almost gets out of hand, and eventually requires 29 steps; the beginner can hardly control these complex cases at all and finishes all of them only after a long struggle (36 or 37 steps) or not at all (second case). The decision space size explodes never for the master, twice for the intermediate, and always (and even quite early) for the beginner.

interventional cardiology. At this stage, the explicit approach adds notions such as strategy, tactic, interventional module, the risk types, etc.

The second stage consists of learning the basic cognitive interventional skills. Based on study of the library cases and initial hands-on experience the trainee learns to design basic interventional strategies based on the specific data. The critical skills here are appropriate evaluation and judgment of all input variables to select suitable access sites and fitting instrumentation and the ability to chain interventional modules in such a manner that indirect risk is avoided, that the strategy is robust against the knowledge risk involved in the initial assessment of the case and against the uncertainty of module

outcomes, and that global parameters such as outcome, total actional risk, procedure time, radiation exposure, material cost etc. are optimized. The trainee learns to chain interventional modules into complete strategies and proceeds from standard to more advanced cases. The trainee is required to explain and to justify the selected strategies and to defend his choices in a dialogue with his mentor.

The main contribution of the explicit approach in this stage is the library of interventional cases. Its first version will serve as the source from which to identify the set of typical interventional modules, subsequent versions will then use those modules as explicit and well-defined terminology.

Combined with hands on training, mastering stages one and two shall enable an interventionist to perform supervised standard interventions effectively, efficiently, and at low total risk.

The third stage consists of learning how to design intermediate and more advanced strategies how to handle unexpected outcomes and how to conduct more complex procedures. Practical training, embodiment of acquired knowledge and development of interventional routines represent the main focus of teaching and learning here. The interventionist learns (still assisted by the mentor) how to decide and act independently. While the knowledge used in stage two consists of a set of heuristic rules and recommendations that are applied and combined in conventional ways, the knowledge used in stage three ads some heuristic rules that are applied and combined in less standard ways in face of higher uncertainty.

Mastering the third stage enables an interventionist to independently perform standard and moderately complex interventions at low risk even when an intervention breaks out of its expected path requiring skilled conduct of non-routine interventions. From this point, continued practice is the road toward becoming an expert interventionist.

CONCLUSIONS

The concept of the explicit knowledge and cognitive skill-based approach has been designed to complement the current mostly tacit and empirical approach to training of cognitive PCI skills. Systematic extraction, codification and transfer of interventional knowledge will enable practitioners to acquire a much larger fraction of their knowledge and skills explicitly, by cognitive learning, rather than relying mostly on tacit modes. We expect that codifying and externalizing PCI knowledge in this manner will help improve both the state-of-the-art and the state-of-practice of the PCI field.

REFERENCES

1. King SB, Aversano T, Ballard WL, Beekman RJ, Cowley MJ, Ellis SG, Faxon DP, Hannan EL, Hirshfeld JW Jr, Jacobs AK, Kimmel MA Jr, Landzberg JS, McKeever LS, Moscucci M, Pomerantz RM, Smith KM, Vetrovec GW. ACCF/AHA/SCAI 2007 update of the clinical competence statement on cardiac interventional procedures: A report of the American college of cardiology foundation/American heart association/American College of physicians task force on clinical competence and training. Available at: http://www.acc.org/qualityandscience/clinical/CIP.pdf.
2. Polanyi M. Personal Knowledge: Toward a Postcritical Philosophy. Chicago: University of Chicago Press; 1974.
3. von Neumann J, Morgenstern O. Theory of Games and Economic Behavior. Princeton, Oxford: Princeton University Press; 1944.
4. Albert A, Peck EA, Wouters P, Van Hemelrijck J, Bert C, Sergeant P. Performance analysis of interactive multimodal CME retraining of attitude toward and application of OPCAB. J Thorac Cardiovasc Surg 2006;131:154–162.
5. Klir GJ. Uncertainty and Information: Foundations of Generalized Information Theory. New Jersey: Wiley-Interscience; 2006.
6. Prechelt L, Lanzer P. The decision-making process in percutaneous coronary interventions. In: Lanzer P, editor. Mastering Endovascular Techniques: Guide to Excellence. Philadelphia: Lippincott, Williams & Wilkins; 2006. pp 103–113.
7. Prechelt L, Lanzer P. On understanding the power of judgement in percutaneous coronary intervention. Clin Res Cardiol 2007;96:1–5.
8. Lanzer P, Prechelt L. On acquiring decision making skills for endovascular interventions. EuroInterv 2008;4:303–305.
9. Williams DO, Baim DS, Bates E, Bost JE, Cowley M, Faxon DP, Feit F. Coronary anatomic and procedural characteristics of patients randomized to coronary angioplasty in the bypass angioplasty revascularization investigation (BARI). Am J Cardiol 1995;75:27C–33C.
10. The TIMI Study Group. The thrombolysis in myocardial infarction (TIMI) trial. N Engl J Med 1985;312:932–941.
11. Sianos G, Morel M-A, Kappetein AP, Morice M-C, Colombo A, Dawkins K, van den Brand M, van Dyck N, Russel ME, Mohr FW, Serruys PW. The SYNTAX score: An angiographic tool grading the complexity of coronary artery disease. EuroInterv 2005;1:219–227.
12. Schmidt W, Lanzer P, Behrens P, Topoleski LDT, Schmitz K-P. A comparison of the mechanical performance characteristics of seven drug-eluting stent systems. Cathet Cardiovasc Interv 2009;73:350–360.
13. Di Mario C, Di Sciascio G, Dubois-Rande J-L, Michels R, Mills P. Curriculum and syllabus for interventional cardiology subspecialty training in Europe. Eurointerv 2006;2:31–36.
14. Wijns W. EAPCI: Education and training programmes in interventional cardiology today. Eurointerv 2007;3:1.
15. Jacobs AK, Faxon DP, Hirshfeld JW Jr, Holmes DR. Task forces 3: Training in diagnostic cardiac catheterization and interventional cardiology. ACC revised recommendations for training in adult cardiovascular medicine core cardiology training II (COCATS 2) (revision of the 1995 COCATS training statement). J Am Coll Cardiol 2002:39:1242–1246.
16. Creager MA, Goldstone J, Hirshfeld JW Jr, Kazmers A, Lorell BH, Pauly RR, Roubin GS, White CJ, Creager MA, Winters WL Jr, Hirshfeld JW Jr, Merli G, Tracy CM. ACC/ACP/SCAI/SVMB/SVS clinical competence statement on vascular medicineand catheter-based peripheral vascular interventions: A report of the American college of cardiology/American heart association/American college of physician task force on clinical competence. J Am Coll Cardiol 2004;44:941–957.
17. van Merrienboer JJG, Kirschner PA. Ten Steps to Complex Learning: A Systematic Approach to Four-Component Instructional Design. New York: Routledge; 2007.

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ORIGINAL PAPER

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Carotid-artery stenting in a high-risk patient population –

single centre, single operator results

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Summary *Aims* The aim of this study was to assess the outcome of carotid-artery stenting (CAS) in high-risk patients in routine clinical settings while excluding the impact of multiple operators and the learning curve of individual operators on the outcome, and to determine the impact of individual risk factors, including vascular multimorbidity, on the outcome. *Methods and results* A total of 143 consecutive patients, 100 (69.9%) males and 43 (30.1%) females, mean age 68.7±8 years treated between February 1999 and May 2004 in the Heart Centre Coswig by a single operator for a symptomatic (n = 37) and asymptomatic (n = 106) on average greater than 70% (82.3 ± 10.7%) or 80% (85.0 ± 9.1%) NASCET carotid-artery stenosis, respectively, were studied. At least one NASCET exclusion criteria was present in 140 patients (97.9%), and vascular multimorbidity was present in 94 (65.7%) patients. In 28 (19.6%) patients there was a complete occlusion of the contralateral internal carotid artery and in 12 (8.4%) patients the procedure was performed prior to emergency coronary bypass surgery. In all, 47 (32.9%) procedures were performed without and 96 (67.1%) were performed with thromboembolic protection. Technical success was achieved in all patients. Combined neurological complications, TIA, PRIND and stroke, occurred in 5 (3.5%) patients, of which 3 (2.1%) were PRIND and 2 (1.4%) were strokes. The neurological complications were more frequent and more severe in symptomatic patients compared to asymptomatic patients (PRIND 2.7% vs 1.9%; stroke 0% vs 5.4%). In patients in whom thromboembolic protection was used, the rate of neurological complications was lower compared to those without protection (PRIND 1.0% vs 4.3%; stroke 1.0% vs. 2.1%). There was no death related to the procedure. Neurological complications were more frequent and more severe in patients with vascular multimorbidity compared to those with an isolated carotid-artery stenosis (4.2% vs 2.0%). The rate of neurological complications was similar in type II diabetics and non-diabetics (2.9% vs 4.1%). In 4.2%, minor complications related to the arterial puncture site were observed (3.5% hematoma not requiring blood transfusion, 0.7% pseudoaneurysm). At follow-up after a minimum of 6 months, 9 (6.3%) patients had died, the majority of whom had died of cardiovascular disease (3.5%). *Conclusions* CAS can be performed with an acceptable risk in high-risk

patients in routine clinical settings when it is performed by an experienced operator. The use of thromboembolic protection devices reduces the risk of neurological complications. Presence of vascular multimorbidity, but not diabetes, appears to increase the risk of all causes and of neurological complications.

Key words
Carotid artery disease – carotid-artery stenting – vascular multimorbidity – diabetes – clinical outcome

Introduction

Carotid-artery stenting (CAS) has recently become an increasingly accepted clinical method to treat carotid artery disease in symptomatic patients with at least 50% and in asymptomatic patients with at least 80% NASCET-stenosis [1]. Indications for CAS typically include patients with high operative risk, post-endarterectomy restenosis, radiation-related stenosis, stenosis in patients with neck dissection, tandem stenosis, stenosis associated with fibromuscular dysplasia, Takayasu arteritis and carotid dissection. Indications for carotid endarterectomy include patients with long and highly irregular stenoses requiring more than two stents, long filiform stenoses and greater than two quadrants highly calcified stenoses, whereas stenoses with high risk of thromboembolisation can be treated by either technique [2]. CAS is associated with a definite risk of death, neurological and puncture site complications which are comparable to those of carotid endartectomy [2–4]. The combined risk of death and neurological complications in CAS appears primarily determined by the patient's risk status and selection criteria [5, 6] the lesion's characteristics [7–9] the use of thromboembolic protection devices [10] and the operator's skills [11]. However, their precise impact on the outcome still remains to be determined.

Here, we report the outcome of a single centre, single operator CAS registry in high-risk patients [12] who were treated for severe symptomatic or asymptomatic internal carotid artery stenosis in routine clinical settings. The impact of accepted risk factors and of vascular multimorbidity [13] on the outcome was assessed.

Methods

Study population

One hundred and forty-three consecutive patients referred between February 1999 and May 2004 to the Heart Centre Coswig with symptomatic internal carotid disease and patients screened for internal carotid disease before coronary bypass surgery or because of significant vascular disease in other vascular territories were evaluated for the presence of significant internal carotid artery disease by color Duplex ultrasonography. In all patients with significant disease by Duplex, selective carotid DSA digital subtraction angiography (DSA) was performed. Indications for treatment were recent neurological symptoms, emergency bypass surgery, subtotal occlusive lesions, high-grade lesions associated with ipsilateral perfusion defects on CT and/or MRI, and contralateral internal carotid occlusion associated in the majority of symptomatic patients with NASCET carotid-artery stenosis > 70%, and in asymptomatic patients with NASCET carotid-artery stenosis > 80%. In each patient, the clinical, non-invasive and invasive findings were evaluated by the interventional cardiologist and the vascular surgeon. Based on set criteria [2], patients were assigned to catheter-based or open-surgery revascularisation. All patients included in this study selected for carotid-artery stenting (CAS) were consecutive cases treated by a single operator (RW).

Study protocol

In all patients studied, the demographic data and the presence of the major cardiovascular risk factors hypertension, diabetes mellitus type II, hypercholesterolemia, smoking and family history of cardiovascular disease, presence of neurological symptoms prior to admission and the presence of vascular disease in the major vascular territories including coronary arteries, abdominal aorta and peripheral arteries, renal arteries and deep peripheral veins were determined. Significant coronary artery disease was considered present in patients with a history of coronary artery bypass surgery, percutaneous coronary intervention or with coronary artery stenosis greater than 50% documented by x-ray coronary angiography. Significant peripheral artery disease was present in patients with a history of aortic and/or peripheral bypass surgery, aortic and/or peripheral artery percutenaous intervention, patients with peripheral artery stenosis greater than 70% documented by arterial DSA or patients with ankle-brachial-doppler index of less than 0.8. Significant renal artery disease was present in all patients with renal artery stenosis greater than 50% on arterial DSA. Deep vein thrombosis was diagnosed in all patients with equivocal documentation by phlebography, duplex sonography, post-thrombotic

syndrome and/or reliable history. Vascular multimorbidity was considered present in patients with a definite disease in at least one additional major vascular territory as defined by the above-stated criteria and in patients with the occluded contralateral internal carotid artery, and/or in patients with cerebrovascular insufficiency as a sign of multivascular cerebral disease. In all patients, modified NASCET exclusion criteria including organ failure or advanced dysfunction (heart, liver, kidney, lungs), unstable cardiac and cerebral vascular symptoms, poorly controlled hypertension and diabetes, history of major recent illness and lesion's characteristics (tandem lesion, restenosis, thrombus, high grade ulceration) were registered [12].

In all patients considered for carotid artery revascularisation, aortic arch and selective bilateral carotid artery digital subtraction angiography (DSA) was performed. The degree of stenosis was judged visually and subsequently quantitively measured utilising the NASCET method [12]. Prior to treatment decision in all patients, cerebral computed tomography and/or magnetic resonance tomography and a complete neurological examination by a neurologist were performed. In patients with indication for carotid artery revascularisation confirmed by a neurologist, the findings were reviewed by an interventional cardiologist and vascular surgeon and the strategy of revascularisation, carotid-artery stenting (CAS), or carotid endarterectomy (CEA), was selected based on a consensus decision. Subsequently, the decision on revascularisation strategy was discussed with the patient and an informed consent was obtained.

Carotid artery stenting (CAS) protocol

Patients were premedicated with 75 mg clopidogrel from the time of decision for CAS. On entry to the catheterisation laboratory, a volume expander infusion was started. All procedures were performed via the femoral artery. Following the puncture 5F sheath was placed, 5000 units unfractioned heparin were given and 5F catheter, typically head hunter configuration was placed in the distal common carotid artery, the lesion and the intracerebral vascular tree were visualised in multiple projections. Subsequently, 0.035″ wire, typically 260 cm Road runner (Cook, Inc.), was advanced into the distal branches of the ipsilateral external carotid artery and the 5F catheter was replaced by 90 cm 7F sheath (Cook, Inc.) with the tip at a safe distance, 2–3 cm, distal to the lesion. In patients with difficult aortic arch anatomy, telescopic approach using the 5F catheter and the 7F sheath was utilised to advance the tip of the sheath distally to the bifurcation. With the sheath securily positioned, the 0.035″ wire was replaced by a soft tip extra support 0.014″ guidewire which was navigated through the stenosis with the tip positioned in the petrose segment of the carotid artery. In patients with extremely tight stenosis, a short low pressure, usually 6 bar, predilatation with a 3.0×30 mm was performed. Following the introduction of the thromboembolic protection devices, which have been standard in all patients since early 2003, in cases where no predilatation was necessary, the 0.014″ wire of the device was used to cross the lesion. The device was deployed distally to the lesion, preferably in a straight segment of the extracranial carotid artery. In the course of the study, AngioGuard (Cordis), NeuroShield (MedNova), EPI Filterwire (Boston Scientific), Accunet (Guidant) and (Spider, ev3) protection devices were utilised. Prior to stent deployment, the patient received 0.5 mg atropin intraveneously with an additional 0.5 mg atropin as needed. Then the stent, typically Wall Stent (Boston Scientific), was placed across the lesion and deployed. To allow for optimal stent apposition, subsequent dilatations with up to 10 mm balloons were performed at the discretion of the operator. Following the stent placement, the blood was vigorously withdrawn from the sheath; the filter device and the sheath were carefully withdrawn and final angiograms in multiple projections taken.

Initially, the patients were monitored during the procedure by a neurologist, later by the operator and the staff. Following the procedure, the patient was brought to an intermediate care unit for 24 hours' monitoring. The sheath was removed when activated clotting time (ACT) was less than 180 s. Clopidogrel was continued and, if there were no complications, the patients were transferred to the ward for another 48 to 72 hour's observation and usually discharged on day four. Patients who developed neurological deficits were evaluated immediately by a neurologist and CT and/or MRI imaging.

Technical success was considered when the lesion had been successfully crossed and revascularised. Procedural success was defined as removal of stenosis without relevant end-organ complications. All patients were evaluated for neurological complications, TIA, PRIND and major stroke, and the arterial puncture site complications, moderate to large hematoma, pseudoaneurysm and fistula, following the procedure and prior to discharge.

Follow-up

At a minimum of 6 months following the procedure, the referring physicians of all patients were contacted by mail and the follow-up regarding occurrence of death and major cardiovascular events (MACE) was completed. In patients who had died, the cause of death was recorded, if known.

Data analysis

In all patients, the demographic data, the major cardiovascular risk factors diabetes type II, hypertension, hypercholesterolemia, family history and smoking, NASCET exclusion criteria, neurological symptoms prior to admission and presence of significant vascular disease in one of the major vascular territories besides carotid arteries, deep vein thrombosis, occluded contralateral carotid artery and chronic cerebrovascular insuffiency, were assessed and analysed. The severity of the carotid-artery stenosis before the procedure was determined from the DSA angiograms according the NASCET method. All complications following the procedure were analysed prior to discharge and at follow-up after a minimum of 6 months.

The statistical analysis of data was performed using software SPSS (version 11.0). Absolute and relative frequencies were calculated. The comparison of independent groups was performed with nonparametric Mann and Whitney U-test.

Table 1 Summary of the five major cardiovascular risk factors

Cardiovascular risk factor	Number of cases	%
Diabetes type II	70	49.0
Hypertension	118	82.5
Hypercholesterolemia	64	44.8
Smoking	28	19.6
Family history	7	4.9

Table 2 Summary of neurological status prior to intervention

Neurological symptoms		Number of cases	%
Absent		106	74.1
Present		37	25.9
	Ischemic insult	15	10.5
	PRIND	4	2.8
	TIA	21	14.7

Results

The data of 143 consecutive patients mean age 68.7 ± 8 years treated between February 1999 and May 2004 in the Heart Centre Coswig with CAS by a single operator were analysed. The primary indication for referral was confirmed or suggested carotid artery disease in 77 (53.8%), carotid and coronary artery disease in 27 (18.9%), coronary artery disease in 11 (7.7%), peripheral artery disease in 2 (1.4%) und miscellaneous indications such as poorly controlled hypertension or diabetes in 22 (15.4%) patients. One hundred (69.9%) patients were males and 43 (30.1%) were females with a mean age of 68.7 ± 8.3 years and 68.8 ± 7.5 years, respectively. In all, 93.0% of patients had at least one cardiovascular risk factor, the most frequent risk factor was poorly controlled hypertension (82.5%), followed by poorly controlled type II diabetes (49.0%). Table 1 summarises the frequency of the five major cardiovascular risk factors in the study population. Among the patients, 106 (74.1%) had no neurological symptoms prior to the admission and 37 (25.9%) were symptomatic (Table 2). Among asymptomatic patients, ipsilateral perfusion defects were documented in 57, subtotal occlusion (> 90%) was present in 48, contralateral internal carotid artery was occluded in 22, and emergency bypass surgery was scheduled in 8. There was no statistically significant difference in the distribution of the cardiovascular risk factors between the groups of the asymptomatic and symptomatic patients. In asymptomatic patients, mean severity of stenoses was 85.0 ± 9.1%, whereas in symptomatic patients it was 82.3 ± 10.7%.

A total of 140 (97.9%) patients had at least one of the NASCET exclusion criteria; three (2.1%) patients had none of the risk factors defined by the NASCET study. Table 3 summarises the distribution of the NASCET risk factors in the study population. Vascular multimorbidity was present in 94 (65.7%) of the patients. Table 4 summarises the occurrence of vascular multimorbidity in the study population.

Thromboembolic protection device was used in 96 (67.1%) of the procedures and there was no statistically significant difference in the distribution of its use between asymptomatic and symptomatic patients. From 1999 through early 2003, thromboembolic protection device had not been used in all patients. Primary indications were high-risk morphology lesion including thrombus, major ulceration and high plaque burden. Since February 2003, all procedures have been device supported.

Technical success was achieved in all patients. Procedural success was achieved in 96.5% of patients. There was no death due to the intervention. Neurological complications occurred in 5 (3.5%) patients, whereas in 6 (4.2%) patients complications of the puncture site occurred with none of them requiring blood transfusion or surgical intervention. Table 5 summarises the overall incidence of neurological and local vascular complications in the entire populations and in subsets of asymptomatic and symptomatic patients. Table 6 summarises the occurrence of TIA, PRIND and major stroke in all patients and

Table 3 Summary of NASCET exclusion criteria in the entire cohort, and in asymptomatic and symptomatic patients

Risik profile (NASCET-criteria)	Total		Asymptomatic		Symptomatic	
	N	%	N	%	N	%
NASCET exclusion criteria Absent	3	2.1	2	1.9	1	2.7
NASCET risk factors Present (≥1)	140	97.9	104	98.1	36	97.3
■ Heart failure	21	14.7	19	17.9	2	5.4
■ Liver failure	0	0.0	0	0.0	0	0.0
■ Respiratory insufficiency	6	4.2	3	2.8	3	8.1
■ Renal insufficiency	20	14.0	17	16.0	3	8.1
■ History of ischemic insult	22	15.4	5	4.7	17	45.9
■ History of cardiac valve replacement	22	15.4	15	14.2	7	18.9
■ History of ipsilateral TEA	11	7.7	9	8.5	2	5.4
■ Diabetes/hypertension[a]	129	90.2	95	89.6	34	91.9
■ Unstabile angina pectoris		26.6	32	30.2	6	16.2
■ Progressive neurological symptoms	13	9.1	6	5.7	7	18.9
■ History of contralateral TEA	1	0.7	1	0.9	0	0.0
■ Major surgical procedure	6	4.2	6	5.7	0	0.0
■ Recent history of neoplasia	5	3.5	4	3.8	1	2.7
■ Ipsilateral restenosis	9	6.3	6	5.7	3	8.1
■ Complicated tandem-stenosis	10	7.0	8	7.5	2	5.4
■ Complicated ulcerated stenosis	21	14.7%	14	13.2	7	18.9
■ Complicated stenosis with thrombus	4	2.8%	3	2.8	1	2.7

[a] Patients with clinically unstable disease

Table 4 Vascular multimorbidity in all patients and in asymptomatic and symptomatic subgroups

Vascular multimorbidity	Total N = 143		Asymptomatic N = 106		Symptomatic N = 37	
	N	%	N	%	N	%
Isolated carotid artery disease	49	34.3	30	28.3	19	51.4
Carotid artery disease with ≥1 additional clinical vascular disease and/or occlusion of the contralateral carotid artery	94	65.7	76	71.7	18	48.6
■ History of coronary bypass/PCI	63	44.1	53	50.0	10	27.0
■ Coronary bypass scheduled within 1–3 days	12	8.4	11	10.4	1	2.7
■ History of peripheral bypass/PTA	29	20.3	23	21.7	6	16.2
■ Renal artery stenosis ≥50% on DSA	20	14.0	15	14.2	5	13.5
■ Cerebrovascular insufficiency secondary to multiple ischemic insults	3	2.1	3	2.8	0	0.0
■ Deep vein lower extremity thrombosis	3	2.1	3	2.8	0	0.0
■ Contralateral carotid artery occlusion	28	19.6	22	20.8	6	16.2

in the asymptomatic and symptomatic subgroups. The occurrence of neurological complications was three times less in patients in whom thromboembolic protection device was used (Table 7).

The risk of overall, neurological and puncture site complications was not statistically different between the patients with type II diabetes mellitus compared to non-diabetics (Table 8). In contrast, the presence of vascular multimorbidity increased the incidence of complications of all causes (9.6% vs 4.1%), and in particular of all neurological complications (4.3% vs 2,0%) (Table 9). Among patients with vascular multimorbidity, the neurological complications were the highest in those with peripheral artery disease, (n = 3, 10, 3%) followed by patients with coronary artery disease, (n = 3, 4.8%). The patent or occluded status of the contralateral carotid artery did not have an impact on neurological complication (3.5% vs 3.6%).

Table 5 Summary of neurological and puncture site complications in the entire cohort, and in the asymptomatic and symptomatic subsets

Overall complications	Total N = 143		Asymptomatic N = 106		Symptomatic N = 37	
	N	%	N	%	N	%
No complications	132	92.3	101	95.3	31	83.8
≥1 any complication	11	7.7	5	4.7	6	16.2
Puncture site	6	4.2	3	2.8	3	8.1
■ Local hematoma	5	3.5	2	1.9	3	8.1
■ Local aneurysm	1	0.7	1	0.9	0	0.0
Neurological	5	3.5	2	1.9	3	8.1
Death prior to discharge	0	0.0	0	0.0	0	0.0

Table 6 Neurological complications in the entire population, and in the asymptomatic and symptomatic subsets

Neurological complications	Total N = 143		Asymptomatic N = 106		Symptomatic N = 37	
	N	%	N	%	N	%
No complications	138	96.5	104	98.1	34	91.9
≥1 complication	5	3.5	2	1.9	3	8.1
■ TIA < 24 h	0	0.0	0	0.0	0	0.0
■ PRIND < 7 days	3	2.1	2	1.9	1	2.7
■ Stroke	2	1.4	0	0.0	2	5.4

Table 7 Frequency and distribution of neurological complications based on the entire cohort, and in subsets with and without thromboembolic protection device

Neurological complications and thromboembolic protection	Total N = 143		With thromboembolic protection N = 96		With thromboembolic protection N = 47	
	N	%	N	%	N	%
No complications	138	96.5	94	97.9	44	93.6
≥1 complication	5	3.5	2	2.1	3	6.4
■ TIA < 24 h	0	0.0	0	0.0	0	0.0
■ PRIND < 7 days	3	2.1	1	1.0	2	4.3
■ Stroke	2	1.4	1	1.0	1	2.1

At follow-up after a minimum of 6 months, 9 (6.3%) patients had died, the majority from heart disease (3.5%). Table 10 shows the frequency of death by cause for the entire populations.

Discussion

Carotid-artery stenting (CAS) carries an acceptable risk of neurological complications even in high-risk patients, when it is performed by an experienced operator. The rate of neurological complications observed in this study was similar to that reported in the literature [1, 14]. In agreement with the published data, the rate of neurological complications was higher in symptomatic compared to asymptomatic patients in this study [15, 16]. Furthermore, in this study, the beneficial effect of thromboembolic protection devices in risk reduction of neurological complications was confirmed in both symptomatic and asymptomatic patients, as previously reported in the literature [17–19]. In this study of high-risk

Table 8 Distribution of overall, neurological and puncture site complications in all patients, and in comparison between type II diabetics and non-diabetics

Overall complications in type II diabetics and non-diabetics	Total N = 143		Type II diabetics N = 70		Non-diabetics N = 73	
	N	%	N	%	N	%
No complications	132	92.3	64	91.4	31	83.8
≥1 any complication	11	7.7	6	8.6	5	6.8
Puncture site	6	4.2	4	5.7	2	2.7
■ Local hematoma	5	3.5	3	4.3	2	2.7
■ Local aneurysm	1	0.7	1	1.4	0	0.0
Neurological	5	3.5	2	2.9	3	4.1
■ TIA < 24 h	0	0.0	0	0	0	0.0
■ PRIND < 7 days	3	2.1	1	1.4	2	2.7
■ Stroke	2	1.4	1	1.4	1	1.4

Table 9 Summary of complications in the entire population, and in patients with and without vascular multimorbidity

Overall complications in patients with vascular multimorbidity	Total N = 143		Vascular multimorbidity N = 94		Isolated carotid artery disease N = 49	
	N	%	N	%	N	%
No complications	132	92.3	85	90.4	47	95.9
> 1 any complication	11	7.7	9	9.6	2	4.1
Puncture site complications	6	4.2	5	5.4	1	2.0
■ Local hematoma	5	3.5	4	4.3	1	2.0
■ Local aneurysm	1	0.7	1	1.1	0	0.0
Neurological complications	5	3.5	4	4.2	1	2.0
■ TIA < 24 h	0	0.0	0	0	0	0.0
■ PRIND < 7 days	3	2.1	2	2.1	1	2.0
■ Stroke	2	1.4	2	2.1	0	0.0

Table 10 Summary of follow-up of all patients, and in asymptomatic and symptomatic subsets, at minimum of 6 months

Outcome at 6 months	Total N = 143		Asymptomatic N = 106		Symptomatic N = 37	
	N	%	N	%	N	%
Total death	9	6.3	7	6.6	3	8.1
■ Cardiovascular (except stroke)	5	3.5	3	2.8	2	5.4
■ Stroke	2	1.4	3	2.8	2	5.4
■ Non-cardiovascular	2	1.4	2	1.9	0	0.0
■ Unknown cause	3	2.1	2	1.9	1	2.7

patients, the presence of type II diabetes did not increase the procedural risk, nor did the presence of the contralateral carotid artery occlusion. Interestingly, in patients with vascular multimorbidity, i.e. definite presence of a clinically relevant disease in at least one additional major vascular territory, the rate of all causes, neurological and punctures site complications was higher. The presence of a definite peripheral artery disease carried a higher risk of complications than the presence of a definite coronary artery disease. Given the high prevalence of vascular multimorbidity in patients typically admitted to heart centres, improved risk stratification prior to CAS by panvascular screening [20] might be justi-

fied. The increased mortality in patients following CAS (6.3%) with the majority of patients dying from heart disease (3.5%) appears to support this notion.

Study limitations

The major limitation of this study is the low number of patients to allow statistical analysis of subsets of patients and factors affecting the outcome. Thus, for example, to allow statistically meaningful definition of the risk of neurological complications due to the presence of a definite peripheral artery disease or coronary artery disease, 300 to 500 patients with a similar risk profile to the studied population would be needed. Similarly, more reliable analysis of outcome of symptomatic and asymptomatic patients would require a more balanced number between these two patient populations.

Another limitation represents heterogeneity introduced by inconsistent use of thromboembolic devices throughout the study. While initially thromboembolic devices were used primarily in high-risk lesions, later in the study they were employed in all patients regardless of the morphological appearance of the lesion. Furthermore, the impact of technical improvements in CAS instrumentation between 1999 and 2004 needs to considered. Thus, transition from 0.035″ to 0.014″ systems allowed the use of low profile dilatation balloon catheters. Development of Carotis-Wall-Stent based on Easy-Wall-Stent was associated with greater radial force and lower less traumatic crossing profile. Market introduction of nitinol based Wall-Stent competitors brought about better selection of stents with differences in tracking ability, radial forces, mesh sizes and longitudinal stability. Similarly, thromboembolic protection devices initially limited to distal occlusion systems have become available in a number of perfusion permitting filters with variable crossing profiles, wall apposition properties, mesh sizes and other variables.

Conclusions

This study documents that carotid-artery stenting (CAS) can be performed with an acceptable risk of neurological complications in unselected high-risk patients routinely referred to a heart centre for coronary and non-coronary revascularisation procedures, provided the procedure is performed by an experienced operator. Neurological examination performed by a neurologist and consensus between the interventionalist and vascular surgeon regarding revascularisation strategy, and stringent neurological follow-up are inseparable components of a routine clinical protocol. Improved risk stratification, including the assessment of the impact of vascular multimorbidity on outcome, is needed to increase the safety of the CAS intervention.

References

1. Yadav JS et al (2004) Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 351:1493–1501
2. Mathias K, Jäger H, Gißler HM (2000) Die endoluminale Therapie der Carotisstenose. Z Kardiol 89(Suppl 8): VIII/19–VIII/26
3. CAVATAS investigators (2001) Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 37:1729–1737
4. Brooks WH, McClure RR, Jones MR et al (2001) Carotid angioplasty and stenting versus carotid endarterectomy: randomized trial in a community hospital. J Am Coll Cardiol 38:1589–1595
5. Shawl F, Kadro W, Domanski MJ et al (2000) Safety and efficacy of elective carotid artery stenting in high risk patiens. J Am Coll Cardiol 35:1721–1728
6. Mathur A, Roubin GS, Iyer SS et al (1998) Predictors of stroke complicating carotid artery stenting. Circulation 97:1239–1245
7. Lovett JK, Gallagher PJ, Hands LJ et al (2004) Histological correlates of carotid surface morphology on lumen contrast imaging Circulation 110:2190–2197
8. Biasi GM, Fronio A, Diethrich EB et al (2004) Carotid plaque echolucency increases the risk of stroke in carotid stenting; The imaging in carotid angioplasty and risk of stroke (ICAROS) study Circulation 110:756–762
9. Spagnoli LC, Mauriello A, Sangiorgi G et al (2004) Extracranial thrombotically active carotid plaque as a risk factor for ischemic stroke JAMA 292:1845–1852
10. Kastrup A, Gröschel K, Krapf et al (2003) Early outcome of carotid angioplasty and stenting with and without cerebral protection devices. A systematic review of literature Stroke 34:813–819
11. Ahmadi R, Willfort A, Lang W et al (2001) Carotid artery stenting: effect of learning curve and intermediate-term morphological outcome J Endovasc Ther 8:539–546
12. North American Symptomatic Carotid Endarterectomy Trial Collaborators (1991) Benefical effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 325:445–453

13. Lanzer P (2003) Vascular multimorbidity in patients with a documented coronary artery disease Z Kardiol 92:650–659
14. Tübler T, Schlüter M, Dirsch O et al (2001) Balloon-protected carotid artery stenting; Relationship of periprocedural neurological complications with the size of particulate debris Circulation 104:2791–2796
15. Roubin GS, New G, Iyer SS et al (2001) Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis: a 5-year prospective analysis. Circulation 103:532–537
16. Minar E, Ahmadi R (2003) Erfahrungen mit der endovaskulären Therapie der Karotisstenose J Neurol Neurochir Psychiatr 4(1):27–32
17. Al-Mubarak N, Roubin GS, Vitek JJ et al (2001) Effect of the distal-balloon protection system on microembolization during carotid stenting Circulation 104:1999–2004
18. Zahn R, Mark B, Nidermaier N et al (2004) Embolic protection devices for the carotid artery stenting: better results than stenting without protection? E Heart J 25:1550–1558
19. Whitlow PL, Lylyk P, Londero H et al (2002) Carotid artery stenting protected with an emboli containment system. Stroke 33:1308–1314
20. Lanzer P, Zuehlke H, Jehle P, Silber R-E (2004) Cardiovascular multimorbidity, emerging coalescence of the integrated panvascular approach Z Kardiol 93:259–265

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ORIGINAL PAPER

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Coronary-like revascularization for atherosclerotic renal artery stenosis –

Results in 181 consecutive patients

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Summary *Aims* The aim of this study was to document the early outcome of coronary-like revascularization for atherosclerotic renal artery stenosis (ARAS). *Methods and results* A total of 181 consecutive patient, 102 men, mean age 66.1 (±9.2) years and 79 females, mean age 68.4 (±9.2) years and 198 lesions were treated between February 1999 and May 2004 for ARAS and retrospectively analyzed. At least one major cardiovascular risk factor was present in 179 (98.9%) patients. Pre-dilatation ARAS was 81.3±9.6%, 27 ARAS were 50–70% and no ARAS was <50%. 135 (68.2%) of the ARAS lesions were ostial and 63 (31.8%) were non-ostial. In 17 (9.4%) patients bilateral ARAS were present. Technical success defined as residual stenosis ≤30% was achieved in 178 (98.3%) of patients and 195 (98.5%) of lesions. In one patient (0.5%) the target ARAS could not be crossed, in two (1.1%) patients residual stenosis was >30%. No major adverse cardiac or cerebral effects were observed. In 3.9% of patients minor local complications of the access site occurred; 4 (2.2%) inguinal hematoma, 3 (1.7%) pseudoaneurysm were documented. Serum creatinine concentrations and systolic and diastolic blood pressure before and after the intervention were not statistically different. *Conclusions* Coronary-like approach to ARAS revascularization is technically feasible and associated with a very low complication rate.

Key words Atherosclerotic renal artery stenosis – renal artery revascularization – precutaneous treatment

Introduction

Renal artery stenosis, RAS, is a common cause of hypertension (renovascular hypertension, RVH), hypertensive nephropathy (HTN), ischemic nephropathy (IN) and renal insufficiency including end stage renal disease. The most common cause of RAS is atherosclerosis (up to 90%) and fibromuscular dysplasia (up to 10%) of patients (for review, see [1]).

Atherosclerotic RAS (ARAS) usually involves the proximal third of the artery, frequently (about 75%) including the ostia. In up to 30% of cases both renal arteries may be stenosed. The rate of progression of ARAS is matter of debate; in one study using duplex classification of renal stenosis severity the cumulative rates of progression from normal to <60% narrowing at 1, 2 and 3 years were 0, 0 and 8% and those from <60% to >60%, 30, 44 and 48%, respectively [2]. Progression of ARAS appears to be associated with a progressive loss of renal tissue [3].

Surgical treatment of ARAS became available in 1973 [4]. At present essentially three different surgi-

cal approaches of revascularization are available: aorto-renal bypass, thromboendearterectomy and reimplantation (for review, see [5]). Although, in the published series the short-term and long-term results of surgical ARAS revascularization have been satisfactory (for review, see [6]) the use of surgery for isolated RAS has rapidly declined with the availability of endovascular treatments.

Renal artery angioplasty was introduced by Grüntzig in 1978 [7]. In early series [8, 9] technical success rates ranged between 75 and 100% in patients with nonostial ARAS; the corresponding rates of medical cure and improvement ranged between 7 to 47% and 31 to 60%, respectively (for review, see [10, 11]). Introduction of renal stents in the early 1990s [12] has improved the procedural safety, extending the interventional spectrum to include ostial lesions [13]. In more recent studies, increasingly low-profile catheter systems have gradually replaced the 0.035 inch – based technology, thus, markedly improving success while lowering the complication rates [14–16].

In accordance with the consensus document for reporting on renal artery revascularization in clinical trials [17], we have retrospectively analyzed the results of ARAS interventions in 181 consecutive patients to document the anatomic success of percutaneous revascularizations. The coronary-like approach defined by the use of small French size coaxial systems typically including 6F guiding catheters, 0.014 inch guidewires, and low-profile rapid-exchange dilatation balloon catheters and stent-delivery systems was employed.

Methods

Data on 181 consecutive patients referred to the Heart Center Coswig for suspected atherosclerotic renal artery stenosis (ARAS) or coronary and/or peripheral artery disease with documented significant ARAS and treated between February 1999 and May 2004 were retrospectively analyzed. Percutaneous revascularization was indicated in patients with ARAS >50% diameter renal artery stenosis and one of the following conditions: poorly controlled hypertension defined as systemic blood pressure >140/90 mmHg despite at least three different blood pressure lowering medications, chronic renal insufficiency defined as elevation of serum creatinine >115 μmol/L, both of the latter two conditions, medically borderline controlled systemic hypertension (≤140/90 mmHg) in the presence of angiographically documented ARAS >80% and hemodynamically significant stenosis. Hemodynamically significant ARAS was considered to be present in patients with >70% diameter narrowing. In borderline stenoses (50–70%), the translesional gradient was routinely measured; mean gradient >10 mmHg was considered significant [17]. Renal artery duplex studies have not been routinely employed.

In all patients the demographic data and the presence of the major cardiovascular risk factors including hypertension, diabetes mellitus type II, hypercholesterolemia, smoking habits and family history of cardiovascular disease were assessed. In addition, the definitive evidence for clinically manifest cardiovascular diseases in other vascular beds was assessed. Vascular multimorbidity was considered in patients with a definitive evidence of vascular disease involving at least two major vascular beds at the time of presentation. Coronary artery disease was considered significant in presence of any of the following: history of coronary artery bypass surgery or catheter-based interventions, coronary angiography with documented stenoses >50% diameter. Significant peripheral arterial disease was present in patients with a history of a peripheral aortic and/or artery bypass and/or peripheral catheter-based intervention, and patients with an ankle-brachial index <0.9. Cerebrovascular disease was considered to be present in patients with a documented medical history of cerebral infarction, carotid artery stenting or Duplex findings of >50% diameter stenosis. Deep vein thrombosis of the lower leg was considered present in patients with a documented disease by Duplex or phlebography. Pulmonary embolization was considered present in patients with a history of the disease documented by pulmonary angiography or scintigraphy. Prior to the procedure in all patients informed consent was obtained based on the established clinical guidelines.

Study protocol

In all patients selective renal artery digital subtraction angiography (RADSA) was performed. The stenosis was measured using the edge-detecting algorithm for quantitative angiography (Philips, Eidhoven, The Netherlands) and the degree of stenosis was calculated as 1 minus the ratio of the diameter of the lumen at the stenosis to the diameter of the lumen of the target renal artery distal to the stenosis both measured in millimeters (mm) multiplied by 100 [13].

The coronary-like approach to ARAS intervention defined by the use of small size introductory sheath, typically 6F, pre-shaped guiding catheters, coronary 0.014 inch guidewires, low profile dilatation balloon catheters and/or stent-delivery devices with rapid-exchange design was employed in all patients. Using the

right common femoral artery and less frequently brachial artery for primary access and sheath placement, the coaxial technique was employed to catheterize the target renal artery. During the early phase the shortened Judkins right or multiple purpose (MP) coronary guides, while later the 50 cm long, renal double curve, RDC, guiding catheters were used. In technically more demanding cases, the telescopic principle utilizing a coaxial diagnostic catheter inside the guide was used to improve steering and stability of the system and to facilitate the engagement of the ostium. Following a stable seating of the guide at the ostium of the target renal artery, RADSA was performed and the degree of ARAS was determined. Subsequently, a coronary 0.014 inch floppy tip, stiff shaft guidewire was employed to navigate the ostium and to cross the lesion. In early stages, primary balloon dilatation was performed. In cases with stentlike results defined as a residual stenosis $<30\%$ in absence of angiographic dissections, stenting was not performed. However, with subsequent improvements and broad availability of the low-profile, rapid exchange technology most ARAS were directly stented using the dedicated (high radial force) peripheral balloon-expansible 4–7 mm diameter and 12–18 mm long stents deployed at high inflation pressures (usually 12 bar). In cases with stent recoil careful after-dilatations with balloons sized to the nominal diameter of the target renal segment were performed. In cases with an extremely tight stenosis or in subtotal occlusions pre-dilatations were performed using 2–3 mm diameter low-profile coronary balloon catheters. To allow precise positioning in ostial lesions strictly ostial orthogonal projections were selected; to this end 30 degrees left and right anterior oblique and anterior-posterior projections were usually acquired. In all cases the attempt was made to position the proximal stent-end to match the inner endovascular interface of the abdominal aorta or to slightly overreach it approximately by one ring of the stent, corresponding typically to 1–2 mm. In all ostial lesions, after-dilatations with oversized balloons were performed to improve the stent to wall adaptation and strut apposition. Subsequently, RADSA were acquired to document the results. In cases with technically successful results considered when residual stenosis was $<30\%$ diameter, the intervention was terminated. In cases with technically suboptimal results additional interventional steps including stent expansions, dilatations of the adjacent segments and necessary a second stent placement were employed. To determine the degree of the residual stenosis, quantitative RADSA measurements were performed as described above.

After the procedure the patients were transferred for up to 12 hours ECG and blood pressure monitoring. In stable patients the sheath was removed usually within 2 hours after the procedure. Creatinine concentration in serum was measured at 2–4, 12 hours and then daily up to the discharge usually on day two after the intervention. In patients with any rise in creatinine, serial creatinine controls were ordered to assure normalization. Blood pressure medication was adjusted to the during the postinterventional period (usually up to two weeks) frequently fluctuating blood pressure values.

Data analysis

In all patients the demographic data, the major cardiovascular risk factors including hypertension, diabetes mellitus, hypercholesterolemia, smoking and family history of cardiovascular diseases and the presence of concomitant clinically relevant coronary artery, cerebrovascular or peripheral vascular disease were assessed. In addition, in all patients renal blood pressure and serum creatinine concentration were measured before and after the intervention. The severity of ARAS was determined as described above. Ostial were considered all lesions <5 mm from the ostial plane. Presence of bilateral ARAS was noted. To determine the anatomical outcome of the interaction the highest degrees of stenosis before and after the intervention were compared. In all patients the presence of major cardiac and cerebrovascular events, MACCE, i.e., myocardial infarction, cerebral ischemia, death and reintervention on the target renal artery as well as presence of bleeding, i.e., minor bleeding not requiring blood transfusion, major bleeding requiring blood transfusion and complications of the access site, i.e., pseudoaneurysm and arterio-venous fistula without or with the need for surgical revision were statistically analyzed. Furthermore, in all patients the total amount of contrast agent used for the initial diagnostics and intervention were assessed. In addition, number of implanted stents per lesion was also determined. Finally, in a subset of patients the amount of contrast agent used, the fluoroscopy time and the radiation exposure used for the ARAS intevention were assessed.

The statistical analysis of data was performed using software SPSS (version 11.0). Absolute and relative frequencies were calculated.

Results

A total of 181 patients, 102 men, mean age 66.1 (± 9.2) years and 79 females, mean ages 68.4 (± 9.2) years were studied. At least one major cardiovascular

risk factor was present in 179 (98.9%) patients. Table 1 shows the distribution of major cardiovascular risk factors among patients. Table 2 summarizes the distribution of vascular co-morbidities.

Indications for ARAS revascularization included poorly controlled hypertension in 84 (46.4%) patients, chronic renal insufficiency in 21 (11.6%) patients, poorly controlled hypertension and chronic renal insufficiency in 24 (13.3%) medically borderline controlled systemic hypertension (≥140/90 mmHg) associated with angiographically documented ARAS >80% in 28 (15.5%) patients and ARAS 50–70% with significant translesional gradient in 24 (13.3%) patients.

In 181 patients 198 lesions were treated. 135 (68.2%) of ARAS lesions were ostial and 63 (31.8%) were non-ostial. In 17 (9.4%) patients bilateral ARAS was present. The mean severity of ARAS was 81.3± 9.6% prior and 2.5± 10.4 after the intervention. Prior to the intervention sixteen 27 stenoses were 50–70%. In 148 (81.8%) of patients and in 33 (18.2%) stent-supported and plain balloon angioplasty were used, respectively. Technical and anatomical success was achieved in 178 (98.3%) of patients. In one patient the target renal artery stenosis could not be crossed with the dilatation balloon and the intervention was terminated after several unsuccessful attempts. In two other cases large plaque burden prevented full stent expansion with the residual stenosis of 78 and 34%. In two patients with a single ARAS each successful revascularization was performed but the angiographic data have been lost. In 196 lesions one stent per lesion was used. In two lesions a second stent was needed to cover a distal dissection and to improve ostial lesion coverage, respectively. Figure 1 shows the distribution of degree of stenoses before and after the intervention.

Table 1 Distribution of major cardiovascular risk factors in the patients studied

Risk profile Any risk factor	No risk factors ≥1 risk factor Unknown	2 179 0	1.1% 98.9% 0.0%
Risk profile Individual risk factors (multiple factors possible)	■ Diabetes ■ Hypertension ■ Hypercholesterolemia ■ Nicotine ■ Family history	81 172 94 47 23	44.8% 95.0% 51.9% 26.0% 12.7%

Table 2 Presence and distribution of co-incident clinically relevant and definitely documented vascular disease in other vascular territories (panvascular status) in the patients studied

Any vascular disease	No ≥1 vascular disease Unknown	102 79 0	56.4% 43.6% 0.0%
Individual vascular diseases (multiple diseases possible)	■ CAD ■ PAD ■ CVD ■ Lower leg deep vein thrombosis ■ Pulmonary embolization	38 9 46 1 1	21.0% 5.0% 25.4% 0.6% 0.6%

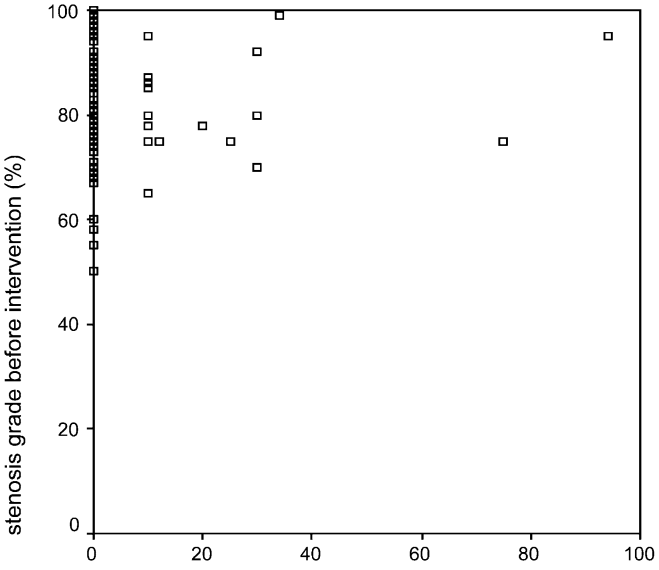


Fig. 1 Distribution of degree of the atherosclerotic renal artery stenoses before and after the intervention in all patients treated

The mean serum creatinine concentration before and after the intervention was 106.7 ± 45.9 μmol/L and 106.1 ± 47.8 μmol/L, respectively; in 40 (22.1%) patients a transient increase in serum creatinine >10% of the baseline value was observed following the intervention. Figure 2 shows the distribution of individual serum concentration levels before and after the intervention. The mean systolic and diastolic blood pressure before and after the intervention were 156 ± 27 mmHg versus 136 ± 21 mmHg and 74 ± 15 mmHg versus 72 ± 13 mmHg, respectively. Figure 3 shows the distribution of individual systolic and diastolic blood pressure measurements before and after the intervention. The differences in serum creatinine, systolic and diastolic blood pressure before and after the intervention did not reach statistical significance. The average amount of contrast media used for the diagnostic evaluations and intervention was 146 ± 91.2 ml (n = 181 patients). In a subgroup of patients the average amount of contrast agent used for ARAS revascularization was 87.2 ± 47.8 ml (n = 51 patients). In addition, the mean fluoroscopy time and radiation exposure was

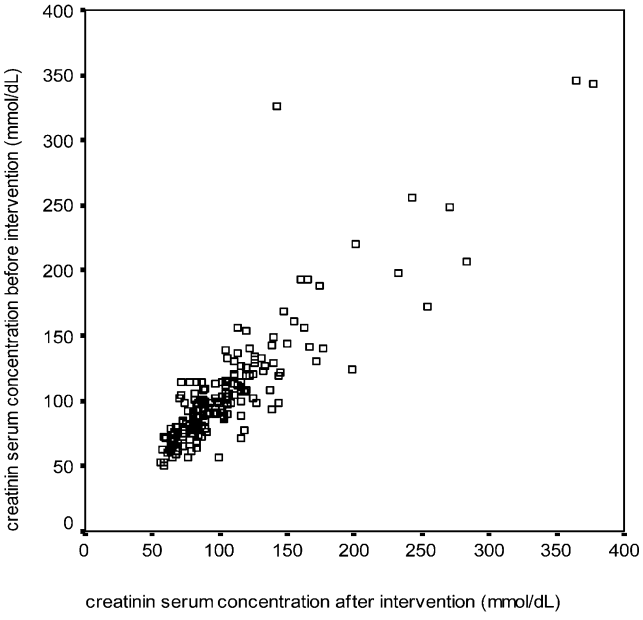
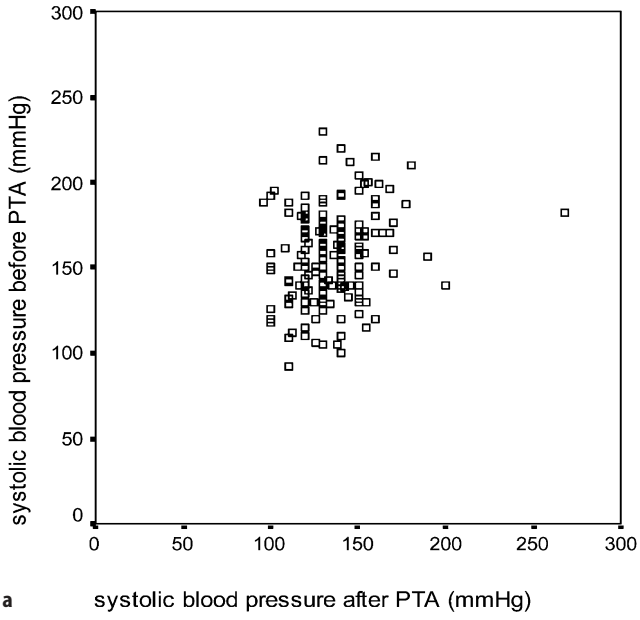


Fig. 2 Distribution of individual serum concentration levels before and after the intervention in all patients treated



a

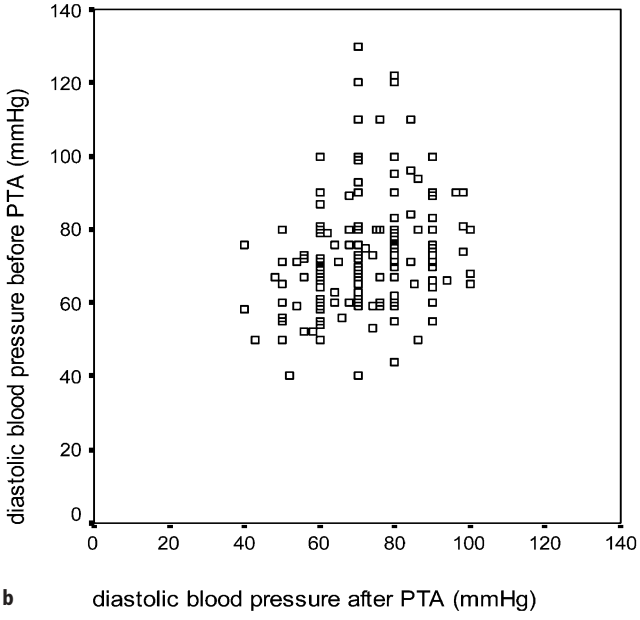


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Fig. 3 Distribution of individual systolic (**a**) and diastolic (**b**) blood pressure measurements before and after the intervention in all patients treated

10.4 ± 7.1 min (n = 49 patients) and 95.8 ± 44.9 cGy/cm^2, respectively.

No major adverse cardiac and cerebral effects were observed. In 3.9% of patients minor local complications of the access site were observed. In 4 (2.2%) patients inguinal hematoma was observed; all patients were treated conservatively, surgical revision or blood transfusion were not required. In 3 (1.7%) patients pseudoaneurysm occurred; ultrasound guided compression was successful in all three patients.

Discussion

The coronary-like approach for ARAS revascularization can be performed with a high technical success and low complication rates in routine clinical settings. To keep the complication rates related to dissections and perforations low careful handling of the guidewire is of particular importance. Specifically, a soft tip 0.014 inch coronary guidewire should be positioned in one of the segmental branches of the renal artery and left steady in place throughout the entire intervention. To avoid proximal dissections with the risk of threatened or actual closure in cases with subtotal ostial stenoses, stable seating of the guide and gentle exploration of the site with a floppy guidewire tip is required. In a large proportion of lesions direct stenting with a low profile stent delivery system is possible and should be performed if technically feasible. If predilatations are needed undersized low profile coronary dilatation catheters of rapid exchange design should be employed. In patients with ostial lesions adaptation of the proximal rings of the stent to the aortic wall using oversized balloons is recommended. In patients with a large plaque burden a complete removal of the stenosis might not be possible, particularly in cases with cir-

cumferential plaque distribution. In these cases, anatomically suboptimal (up to 40% diameter residual stenosis) but functionally adequate (0 mmHg translesional pressure gradient) seem acceptable. Using low-profile catheter based technology, similarly favorable results have been reported previously by others [18] endorsing the results of this study. The results achievable when miniaturized coronary-like techniques and technology are used are strikingly improved compared to earlier results reported from the use of the more robust instrumentation, mostly using the 0.035 inch techniques and technology, customary in peripheral interventions up to the late 1990s [19]. The use of more than one stent per lesion either to cover a dissection or to improve the results appears rare (1% in this study). In rare cases with non-dilatable lesions due to high plaque burden and/or high circumferential rigidity and in rare cases with non-crossable lesions, open surgery ARAS revascularization may still provide a reasonable alternative in selected patients. Bilateral ARAS are relatively frequent (9.4% of patients in this study) and both lesions can be safely treated in one setting.

The availability of stable high technical success low overall risk revascularization techniques utilizing the coronary-like approach provides an excellent starting point for future trials designed to study the question of the clinical impact of ARAS revascularization in different subsets and patients populations.

Study limitations

The major limitation of this study was lack of a complete battery of postprocedural tests to assess subclinical complications such as small renal infarcts and disseminated embolizations. Thus, serial assessments of serum levels of lactate dehydrogenase, eosinophilia and hypocomplementemia and routine evaluations of urine sediment for the presence of cells or casts, hematuria and red cell casts, and proteinuria as indirect laboratory findings suggestive of renal infarctions and/or embolizations have not been performed (for review see [20]). In addition, the patency of the target renal artery and the degree of restenosis was not assessed on a long-term follow-up required to fully validate the described approach. However, the rates of in-stent restenosis following stent-supported angioplasty for ARAS have been abundantly reported in the literature and show consistent results (for review see [19]). In a recent study, restenosis rate for in-stent restenoses ≥50% diameter was 17.4% [15].

Conclusions

The study demonstrates that the coronary-like approach to ARAS revascularization can be performed with high success and low complication rates. This stable and now established technique of renal artery stenosis revascularization appears to be well suited for clinical trials evaluating the impact of improved renal perfusion on renal function and blood pressure in the concerned, usually high-risk populations.

References

1. Murphy TP, Cooper CJ, Dworkin LD et al (2005) The Cardiovascular Outcomes with Renal Atherosclerotic Lesions (CORAL) Study: Rationale and Methods. J Vasc Interv Radiol 16:1295–1300
2. Zierler RE, Bergelin RO, Davidson RC et al (1996) A prospective study of disease progression in patients with atherosclerotic renal artery stenosis. Am J Hyperten 9:1055–1061
3. Strandness ED Jr (1994) Natural history of renal artery stenosis. Am J Kidney Dis 24:630–635
4. Freeman N (1973) Thromboendarterectomy for hypertension due to due to renal artery occlusion. JAMA 157:1077–1083
5. Stanley JC (2002) Renal vascular diseases: Surgical therapy. In: Lanzer P, Topol EJ (eds) PanVascular medicine: Integrated clinical approach. Springer, Berlin New York, pp 1798–1808
6. Hasen JK, Dean RH (2002) Renovascular disease. In: Moore WS (ed) Vascular surgery: A comprehensive review, 6th edition. WB Saunders Company, Philadelphia, pp 548–569
7. Grüntzig A, Kuhlmann U, Vetter W (1978) Treatment of renovascular hypertension with percutaneous transluminal dilatation of a renal artery stenosis. Lancet 1:801–802
8. Schwarten DE, Yune HY, Klatte EC et al (1980) Clinical experience with percutaneous transluminal angioplasty (PTA) of stenotic renal arteries. Radiology 135:601–604
9. Tegtmeyer CJ, Ayers CA, Wellons HA (1980) Axiallary approach to percutaneous renal artery dilatation. Radiology 135:775–776
10. Trost DW, Sos TA (1998) Renal artery angioplasty and stent placement: Indications and results. In: Perler BA, Becker GJ. Vascular intervention: A clinical approach. Thieme, New York Stuttgart, pp 575–583

11. Kaplan NM, Rose BD (2005) Treatment of unilateral renal artery stenosis. *http://patients.uptodate.com/topic.asp?file=hyperten/16017 title = Renal + artery + Stenting* (accessed December 28, 2005)
12. Dorros G, Prince C, Mathiak L (1993) Stenting of renal artery stenosis achieves better relief of the obstructive lesion than balloon angioplasty. Cathet Cardiovasc Diagnost 29:191–198
13. Blum U, Krumme B, Flügel P et al (1997) Treatment of osteal renal artery stenosis with vascular endoprothesis after unsuccesful balloon angioplasty. N Engl J Med 336:459–465
14. Zeller T, Frank U, Müller C et al (2003) Predictors of improved renal function after percutaneous stent-supported angioplasty of severe atherosclerotic ostial renal artery stenosis. Circulation 108:2244–2249
15. Rocha-Singh K, Jaff MR, Rosenfield K for the ASPIRE-2 Investigators (2005) Evaluation of safety and effectiveness of renal artery stenting after unsuccessfull balloon angioplasty: The ASPIRE-2 Study. J Am Coll Cardiol 46:776–832
16. Nolan BW, Schermerhorn ML, Rowell E et al (2005) Outcomes of renal artery angioplasty and stenting using low-profile systems. J Vasc Surg 41:46–52
17. Rundback JH, Sacks D, Kent C et al for the American Heart Association Council on Cardiovascular Radiology, High Blood Pressure Research, Kidney in Cardiovascular Disease, Cardio-Thoracic and Vascular Surgery, and Clinical Cardiology, and the Society of Interventional Radiology FDA Device Forum Committee (2002) Guidelines for the reporting of renal artery revascularization in clinical trials. Circulation 106:1572–1585
18. Nolan BW, Schermerhorn ML, Rowell E et al (2005) Outcomes of renal artery angioplasty and stenting using low-profile systems. J Vasc Surg 41:46–52
19. Lim ST, Rosenfield K (2000) Renal artery stent placement: Indications and results. Curr Interv Cardiol Rep 2:130–139
20. Rose BD, Tunick PA (2005) Clinical characteristics of renal atheroemboli. *http://patients.uptodate.com/topic.asp?file = renldis/16306title = Renal + atheroemboli* (accessed December 30, 2005)

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ORIGINAL PAPER

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Intentional single-stage revascularization of two different vascular beds in patients with vascular multimorbidity

A feasibility study

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Abstract *Aims* The aim of this retrospective study was to assess the feasibility of catheter-based interventions in two different vascular beds performed in a single stage in patients with vascular multimorbidity. *Methods and results* Fifty patients, 28 males, mean age 68.6 (±9.2) years and 22 females, mean ages 72.2 (±6.4) years were studied. At least one major cardiovascular risk factor was present in 48 (94%) of all patients. The most frequent combination of interventions was coronary artery disease (CAD) and renovascular disease (RVD) (20 patients, 40%) followed by CAD and peripheral artery disease (PAD) (17 patients, 34%). In all patients technical success, defined as residual stenosis ≤30% diameter, and procedural success, defined as lack of major adverse cardiac and cerebrovascular events (MACCE) during the in-hospital period, were achieved. In two patients surgical revision of the access site was required and in two additional patients minor local bleeding was observed. *Conclusions* Sequential vascular interventions in different vascular beds may be performed in a single stage with high success rates, however, compared to historical controls possibly at a higher rate of access site complications. A larger study using controls is needed to assess the medical benefits and cost efficacy of a single stage approach in patients with clinically relevant vascular multimorbidity.

Key words
endovascular treatment – vascular multimorbidity – feasibility study

Introduction

Atherosclerosis is a systemic vascular disorder frequently involving multiple vascular beds [1]. Vascular multimorbidity can be defined as presence of clinically relevant disease in at least two major vascular territories manifest at the same time in a single patient [2]. A typical example of vascular multimorbidity is a patient with intermittent claudication (peripheral arterial disease (PAD)) and angina (coronary artery disease (CAD)). Clinical presentation of vascular multimorbidity is usually dominated by the symptoms related to one of the ischemic organs, partially or completely masking symptoms related to ischemia in other organs. Recognition of vascular multimorbidity is important to allow treatment and it is critical in patients undergoing major vascular and non-vascular surgery for risk stratification [3]. A typical example is a patient with symptomatic CAD and significant carotid artery disease scheduled for coronary artery bypass surgery.

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At present, patients with vascular multimorbidity, when detected, will be treated by coronary or vascular surgeons or interventionists based in cardiology, radiology, neuroradiology or other medical subspecialty programs depending on the topographic distribution of the vascular disease and locally available expertise. However, because of the multiplicity of specialists participating in treatments of these patients the treatments are heterogeneous and frequently based on variable principles and standards [4].

Endovascular therapy is by its very principle multiterritorial: establishing a single arterial access opens the "door" for interventions at multiple sites along the selected vascular pathways [5]. However, despite this unique advantage, intentional systemic revascularization (ISR) treatments have been rarely utilized in clinical settings. In fact only scattered publications, mostly case reports, are available in the literature [6, 7].

In this study we evaluated the technical feasibility of single stage endovascular interventions in patients with documented critical vascular multimorbidity.

Methods

Fifty patients admitted to the Heart Centre Coswig between May 2001 and November 2004 with vascular multimorbidity were treated by single stage endovascular interventions involving two major vascular beds were retrospectively studied. Major vascular beds were considered carotid, coronary, iliac, lower extremity and renal arteries and the aorta. In all patients the vascular disease was considered significant based on the following criteria: CAD – documentation of myocardial ischemia by ergometry or dobutamine stress echocardiography testing and ≥70% coronary artery stenosis in the related coronary artery by angiography; cerebrovascular disease (CVD) – documentation of cerebral infarction by history and CT- or MR-imaging in presence of ≥70% ipsilateral internal carotid artery stenosis documented by angiography and determined using NASCET method [8]; renovascular disease (RVD) – documentation of a systemic hypertension suboptimally controlled on triple antihypertensive medication and/or chronic renal insufficiency in presence of ≥50% ipsilateral renal artery stenosis [9]; aortic and peripheral arterial disease (PAD) – documentation of intermittent claudication ≥ Fontaine II b in presence of ≥70% ipsilateral aortic, iliac, femoral, popliteal or infrapopliteal artery stenosis. The suitability of patients for single stage intervention was decided by the operator based on clinical grounds. Prior to the procedure in all patients informed consent was obtained according to the guidelines.

Study protocol

In all patients the demographic data and the presence of the major cardiovascular risk factors including hypertension, diabetes mellitus type II, hypercholesterolemia, smoking habits and family history of cardiovascular disease were assessed. In addition, the presence of clinically manifest cardiovascular diseases in other vascular beds was assessed. Revascularizations were performed using the standard approach established for each vascular territory in our laboratory [10–12]. Typically, 6F systems were primarily used but in some patients multiple exchanges of sheaths were necessary. In patients with CAD usually coronary interventions were performed first followed by non-coronary procedures. In two patients without CAD the peripheral arterial intervention was performed first. All patients were treated according to standard clinical protocols; no special precautions or considerations during the periinterventional period were taken. After termination of the procedure typically the patients were transferred for up to 12 hours ECG and blood pressure monitoring. In stable patients the sheath was removed usually within 2 hours after the procedure. Creatinine concentration in serum was measured 2–4, 12 hours and then daily up to the discharge usually on day two after the intervention. In patients with any rise in creatinine ≥10% serial controls were ordered to assure return to baseline.

Data analysis

In all patients the demographic data, the major cardiovascular risk factors including hypertension, diabetes mellitus, hypercholesterolemia, smoking and family history of cardiovascular diseases were noted. Quantitative measurements of the stenosis severity determined in percent of diameter of a non-stenotic were performed from cine single frame images in patients with CAD, and from digital subtraction angiograms (DSA) in patients with PAD, CVD and RVD according to the established standards. Technical success was considered to be present when residual stenosis in any territory was <30% diameter. Procedural success was considered to be present when no major adverse cardiac and cerebrovascular events (MACCE) occurred during hospitalization. To characterize the single stage-two territories intervention the length of the hospital stay in days, length of the procedure in minutes defined as the time from

positioning the patient at the table up to the termination of the procedure, fluoroscopy time, radiation dose and material costs for each patient were noted. Any complications associated with the procedure up to discharge were reported. Specifically, the presence of a minor bleeding not requiring blood transfusion, major bleeding requiring blood transfusion, surgical interventions and MACCE complications were recorded. The statistical analysis of data was performed using software SPSS (version 11.0). Absolute and relative frequencies were calculated. The comparison of independent or dependent groups was performed with nonparametric test by Mann and Whitney or Wilcoxon, respectively.

Results

Fifty patients – 28 males, mean age 68.6 (±9.2) years and 22 females, mean ages 72.2 (±6.4) years – were studied. At least one major cardiovascular risk factor was present in all patients. Table 1 shows the distribution of major cardiovascular risk factors in studied patients. In 48 (96%) one of the two interventions involved the coronary arteries. The most frequent combination of interventions was CAD and RVD (20 patients, 40%) followed by CAD and PAD (17 patients, 34%). The average severity of CAD, CVD, RVD and PAD stenoses was 78±7, 81±12, 68±9 and 75±10%. Technical and procedural success was achieved in all patients (100%). In two patients surgical revision for a large pseudoaneurysm was required and in two patients minor bleeding occurred. Table 2 shows the distribution of all in-hospital complications associated with the access site. Table 3 summarizes the feasibility data for each combination of the single stage multiterritory interventions. Figs. 1 and 2 show comparisons between combined interventions performed in patients with CAD and CVD, or PAD, or RVD.

Table 1 Distribution of major cardiovascular risk factors in 50 patients with vascular multimorbidity

Major cardiovascular risk factors absent.	2	4%
≥1 risk factor	48	96%
Risk profile (including multiple entries)		
Diabetes	21	42%
Hypertension	44	88%
Hypercholesterolemia	40	80%
Nicotine	10	20%
Family history	4	8%

Discussion

To our knowledge this is the first study demonstrating the technical and procedural feasibility of combined interventions in a single stage in patients with vascular multimorbidity in a larger cohort of patients. The data show that interventions in different vascular beds may be combined and performed with high technical and procedural success rates in single stage.

Based on this preliminary evidence it appears that the success rates of single stage multivascular terri-

Table 2 Incidence of all in-hospital complications of the access site observed in all patients in this study

Vascular territory targeted by the interventions	N	Bleeding without blood transfusion		Bleeding requiring blood transfusion		Surgical revison	
		N	%	N	%	N	%
PAD + CVD	1	0	0	0	0	0	0
PAD + RVD	1	0	0	0	0	0	0
CAD + PAD	17	0	0	0	0	1	6
CAD + CVD	10	0	0	0	0	0	0
CAD + RVD	20	1	5	0	0	1	5
CAD + RVD + PAD	1	0	0	0	0	0	0

PAD peripheral arterial disease, *CAD* coronary artery disease, *CVD* cerebrovascular disease, *RVD* renovascular disease

Table 3 Feasibility data for 47 out of 50 studied patients with vascular multimorbidity and combined single stage revascularizations

Interventions in vascular territories	Number of patients	Fluoroscopy time (min±SD)	Duration of procedure (min±SD)	Radiation dose (Gy/cm^2)	Length of hospital stay (days±SD)	Material costs (€±SD)
CAD+PAD	17	22.1±17.6	96.7±40.9	146.7±74.5	7.4±6.2	1525.17±832.39
CAD+CVD	10	22.0±9.0	103.4±29.0	79.4±24.7	9.1±5.2	3022.22±989.28
CAD+RVD	20	21.0±9.8	83.0±31.8	135.5±58.2	7.4±4.8	1904.19±716.13

CAD coronary artery disease, *PAD* peripheral arterial disease, *CVD* cerebrovascular disease, *RVD* renovascular disease, *Gy* Gray, *SD* standard deviation, € euro currency. Three patients, one with PAD+CVD, one with PAD+RVD and one with CAD+RVD+PAD were not included because no statistical means could be obtained

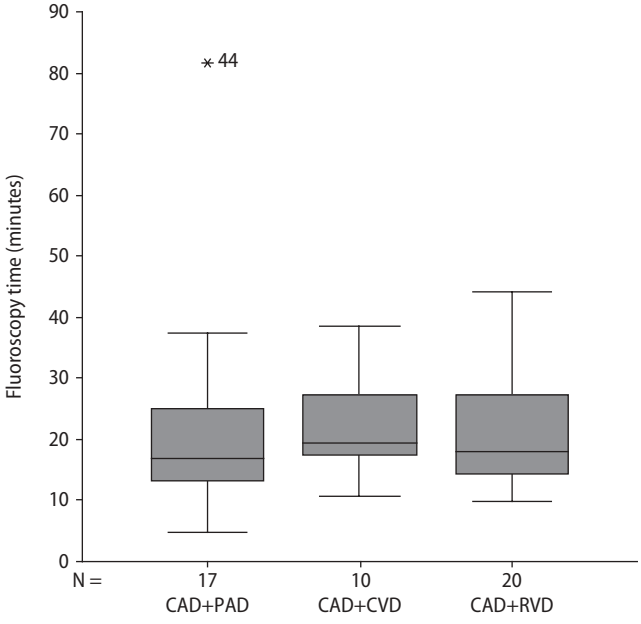

Fig. 1 Fluoroscopy time (mean and standard deviation) in 47 patients with single stage percutaneous interventions for coronary artery (CAD) and peripheral arterial disease (PAD) or cerebrovascular disease (CVD) or renovascular disease (RVD) observed in this study

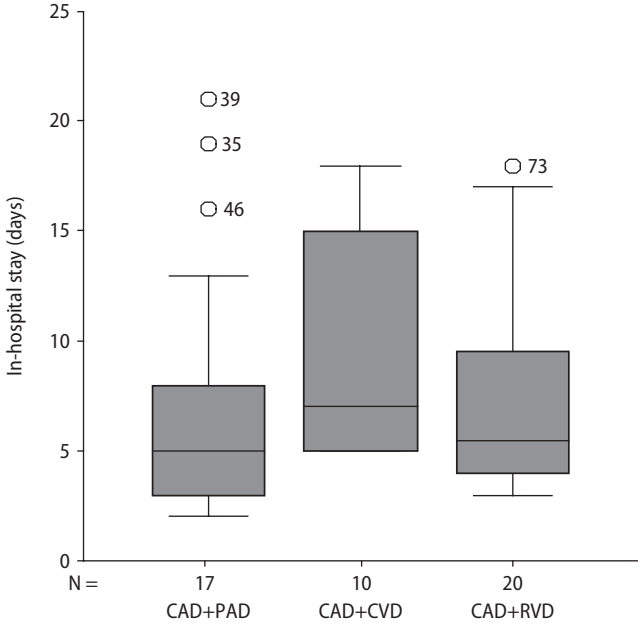

Fig. 2 Hospital stay (mean and standard deviation) in 47 patients with single stage percutaneous interventions for coronary artery (CAD) and peripheral arterial disease (PAD) or cerebrovascular disease (CVD) or renovascular disease (RVD) observed in this study

tory interventions are comparable to those observed in staged procedures, thus potentially reducing the overall risk. For example, in our own series technical and anatomical success were achieved in 178 (98.3%) of patients with atherosclerotic renal artery stenosis [11]. Similarly, in patients with stent-angioplasty for internal carotid stenosis the procedural success was achieved in 96.5% of patients [10].

In this preliminary study, two patients required surgical intervention for pseudoaneurysm repair. For comparison in our previous studies the rate of access site complications was 4.2 and 3.9%, respectively, but no patients needed blood transfusion or surgery [10, 11]. Longer intervention and longer intravascular sheath residence times, as well as multiple exchanges of sheath may be in part responsible for these access site complications. In this study the sheath was left in place in all patients following the intervention to increase safety in case of complications. In none of the patients was a closure device used. Early sheath removal and use of closure devices may reduce access site complications.

The major drawbacks of single stage multi-territory procedures may place greater demands on the patient and on the interventionists due to a longer procedural time compared to the standard staged approach. Greater practice and greater compatibility of endovascular instrumentation may reduce procedural duration.

Study limitations

The major limitation of this study is its retrospective character and the lack of randomized controls for comparisons. Historical controls from our laboratory (unpublished data) indicated a mean duration of percutaneous coronary interventions of 49.3 ± 28.9 min (n = 148 procedures) and for peripheral arterial interventions 66.8 ± 41.9 min (n = 103 procedures) (unpublished data). This limited comparison would for example suggest a savings of approximately 19 min or 16% (116 versus 97 min) less procedure time in patients with CAD and PAD if both vascular territories were revascularized in a single stage rather than in staged procedures. However, direct comparisons based on larger population of patients are needed to determine the real clinical merits and the cost efficacy of single stage procedures in patients with vascular multimorbidity.

Conclusions

The study demonstrates that catheter-based interventions in two vascular beds can be performed safely and with high success rates in a single stage. With now documented feasibility of single stage multiple vascular territory interventions more comprehensive

comparisons of the standard and the proposed approach in a larger population of patients appear justified.

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References

1. McGill H Jr (ed) (1968) The geographic pathology of atherosclerosis. Lab Invest 18:465–639
2. Lanzer P (2003) Vascular multimorbidity in patients with a documented coronary artery disease. Z Kardiol 92:650–659
3. Eagle KA, Berger PB, Calkins H, et al (2002) ACC/AHA Guideline Update for Perioperative Cardiovascular Evaluation for Noncardiac Surgery – Executive Summary. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation 105:1257–1267
4. Lanzer P, Topol EJ (2002) Introduction. In: Lanzer P, Topol EJ (eds) PanVascular Medicine; Integrated clinical management. Springer, New York, pp
5. Lanzer P (ed) (2006) Mastering endovascular techniques; Guide to excellence. Lippincott Williams & Wilkins, Philadelphia, pp
6. Klez RS, Rozek MM, Bouknight D (2001) Bilateral carotid stenting combined with three-vessel percutaneous coronary intervention in single sitting. Cathet Cardiovasc Diagn 52: 100–104
7. Baruah DK, Panigraphi NK, Srinivas AN (2003) Concurrent coronary, bilateral iliac and left renal artery direct stenting. Ind Heart J 55:71–74
8. Young GR, Humphrey PRD, Nixon TE, Smith ETS (1996) Variability in measurements of extracranial internal carotid artery stenosis as displayed by both digital subtraction and magnetic resonance angiography. Stroke 27:467–473
9. Blum U, Krumme B, Flügel P et al (1997) Treatment of osteal renal artery stenosis with vascular endoprothesis after unsuccessful balloon angioplasty. N Engl J Med 336:459–465
10. Lanzer P, Weser R, Prettin C (2006) Carotid-artery stenting in a high-risk patient population – single centre, single operator results. Clin Res Cardiol 95:4–12
11. Lanzer P, Weser R, Prettin C (2006) Coronary-like revascularization for renal artery stenosis – Results in 181 consecutive patients. Clin Res Cardiol 95:1–7
12. Lanzer P, Weser R (2006) Aortoiliac and lower extremity arteries. In: Lanzer P (ed) Mastering endovascular techniques; Guide to excellence. Lippincott Williams & Wilkins, Philadelphia, pp 337–385