Einfluss einer präoperativen perkutanen Koronarintervention auf den Therapieerfolg von Patienten nach koronarer Bypassoperation

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Abkürzungsverzeichnis

CABG	Aorto-koronare Bypass-Operation (Coronary Artery Bypass Graft = CABG)
CCS	Klassifikationssystem der Canadian Cardiovascular Society
CVVH	Kontinuierliche veno-venöse Hämofiltration
CVVHD	Kontinuierliche veno-venöse Hämodialyse
EACTS	European Association for Cardio-Thoracic Surgery
ECMO	Extrakorporale Membranoxygenierung
EK	Erythrozytenkonzentrat
EQ-5D-3L	Fragebogen zur Bewertung der Lebensqualitiät (European Quality-of-Life–5 Dimensions and 3 Levels Health Questionnaire)
ESC	European Society of Cardiology
EuroScore II	Bewertungssystem zur Mortalitätsvorhersage vor kardiochirurgischem Eingriff (European System for Cardiac Operative Risk Evaluation II)
FFP	Gefrorenes Frischplasma (Fresh Frozen Plasma)
IABP	Intraaortale Ballonpumpe
ICD	International Statistical Classification of Diseases and Related Health Problems (Internationale Klassifikation der Krankheiten)
KHK	Koronare Herzkrankheit
LAD	Left Anterior Descending Artery Synonym: Ramus interventricularis anterior (RIVA)
LM	Hauptstamm (Left Main Coronary Artery)
MI	Myokardinfarkt

NSAR	Nicht steroidale Antirheumatika (Non-Steroidal Anti-Inflammatory Drugs = NSAID)
NSTEMI	Nicht-ST-Hebungsinfarkt (Non-ST-Segment Elevation Myocardial Infarction)
NYHA	Klassifikationssystem der New York Heart Association
PAVK	Periphere arterielle Verschlusskrankheit (Peripheral Arterial Occlusive Disease = PAOD)
PCI	Perkutane Koronarintervention
QoL	Lebensqualität (Quality of Life)
SAPS II	Punkte-Bewertungssystem zur Einschätzung des Aufwands der intensivmedizinischen Behandlung (Simplified Acute Physiology Score II)
SD	Standardabweichung (Standard Deviation)
STEMI	ST-Hebungsinfarkt (ST-Elevation Myocardial Infarction)
STS	Bewertungssystem für Mortalität und Morbidität (Society of Thoracic Surgeons)
SYNTAX	Angiographisches Bewertungssystem zur Einordnung der Komplexität der KHK (SYNergy between PCI with TAXus and Cardiac Surgery)
TISS-10	Punkte-Bewertungssystem zur Einschätzung des Aufwands der intensivmedizinischen Behandlung (Therapeutic Intervention Scoring System)
TK	Thrombozytenkonzentrat

1. Deutsche Zusammenfassung

1.1 Einleitung

Nach den Daten des statistischen Bundesamtes ist die häufigste Todesursache in Deutschland (im Jahr 2021) eine Herz-Kreislauferkrankung (33,3 %) (Statistisches Bundesamt, 2022). Hiervon wiederum ist die häufigste ICD-Codierung bei den Verstorbenen die chronische ischämische Herzkrankheit und macht damit beinahe 22 % im Jahr 2021 aus (Statistisches Bundesamt, 2022).

Nicht nur in Deutschland sondern weltweit ist die koronare Herzkrankheit (KHK) seit Jahrzehnten eine der führenden Ursachen für Morbidität und Mortalität (Heidenreich, 2011; Townsend et al., 2022). Gleichzeitig bedeutet dies eine hohe finanzielle Belastung für das Gesundheitssystem aufgrund häufiger und teils längerer Krankenhausaufenthalte inklusive hoher Behandlungskosten (Heidenreich et al., 2011). Die optimale und frühzeitige Revaskularisierung für die betroffenen Patienten ist daher als essenziell anzusehen, nicht nur für die Verbesserung der Lebensqualität der Patienten, sondern auch für die Kostenoptimierung des Gesundheitssystems.

Für die Behandlung der koronaren Herzkrankheit ist die Standardtherapie die Revaskularisierung. Diese erfolgt mittels perkutaner koronarer Intervention (PCI) oder operativer Bypassversorgung (CABG). Zur Entscheidung, welche Form der Revaskularisierung für den individuellen Patienten in Frage kommt, haben die Europäische Gesellschaft für Kardiologie (ESC) und die Europäische Vereinigung für Herz- und Thoraxchirurgie (EACTS) Leitlinien zur Myokardrevaskularisation erarbeitet (Neumann et al., 2019).

In den Leitlinien findet sich der SYNTAX-Score (SYNergy between PCI with TAXus and Cardiac Surgery) als eines der wichtigsten Instrumente zur Entscheidungsfindung hinsichtlich der Revaskularisationsstrategie (Farooq et al., 2013; Bundhun et al., 2017; Thuijs et al., 2019; Banning et al., 2021).

Die Entwicklung der letzten Jahre zeigt eine Tendenz hin zur häufigeren perkutanen Revaskularisierung (Kolh et al., 2014). Aufgrund von vergleichbarer Studienergebnisse von PCI und CABG bei komplexer Koronaranatomie erfolgt auch hier immer häufiger die

PCI - das aber nicht nur bei Patienten mit niedrigem Risiko, sondern auch bei Hochrisikopatienten (komplexe KHK, Diabetes mellitus) (Farkouh et al., 2012; Ohlmeier et al., 2016). Diesem Umstand geschuldet hat die Herzchirurgie immer komplexere Operationsbedingungen bei ansteigender Patientenzahl mit vorheriger PCI (Head et al., 2013). Die Zahlen variieren je nach Studie: Ca. 10-30 % der Patienten, die zur Bypassoperation vorgestellt werden, hatten vorher eine Koronarangiographie mit Intervention (O'Brien et al., 2018). In unserer Studie waren es 21,36 %. Hierbei führen wiederholte perkutane Koronarinterventionen zu einer Verzögerung der vollständigen Revaskularisierung und folglich zu einer wiederholten Hospitalisierung (Filardo et al., 2001).

Eine präoperative perkutane Koronarintervention ist bereits als Risikofaktor für die koronare Bypass-Chirurgie in verschiedenen Studien beschrieben worden (Frutkin et al., 2009). Es wurde daher in der Vergangenheit bereits versucht, den prognostischen Einfluss einer vorangegangenen PCI vor CABG zu analysieren. Weiterhin ist dies aber schwer zu erfassen (Miguel et al., 2020).

1.1.1 Fragestellung

Ziel der Dissertationsarbeit war es, herauszuarbeiten, ob eine präoperative PCI bei Patienten nach aortokoronarer Bypassoperation Einfluss auf das postoperative Ergebnis hat und dies insbesondere auch im Hinblick, ob die vorangegangene PCI leitlinienkonform, gemessen an den ESC-Leitlinien von 2014, oder nicht-leitlinienkonform erfolgte (Hamiko, Konrad et al., 2023).

1.2 Material und Methoden

1.2.1 Patienten und Gruppierung

In dieser retrospektiven Analyse betrachteten wir die Daten von 997 Patienten, die sich zwischen 2014-2016 in der Herzchirurgie des Universitätsklinikums Bonn einer isolierten aortokoronaren Bypassoperation unterzogen haben.

Das Patientengut wurde zunächst in zwei Gruppen eingeteilt in Abhängigkeit davon, ob präoperativ eine perkutane Koronarintervention vorausgegangen war: PCF („PCI-First“) – Patienten mit vorheriger PCI innerhalb von 3 Jahren präoperativ (n=215) und CO („CABG-only“) – Patienten ohne vorherige PCI (n=784) (Hamiko, Konrad et al., 2023).

Hiernach erfolgte eine Subgruppierung der PCF–Gruppe: Die Patienten, die nach ESC/EACTS-Leitlinie (2014) leitlinienkonform koronarinterveniert wurden, bildeten eine Subgruppe (GCO=guideline-conform, n=67). Die zweite Subgruppe wurde folglich aus den nicht-leitlinienkonform intervenierten Patienten gebildet (GNC=guideline-nonconform, n=24) (Hamiko, Konrad et al., 2023).

Die Divergenz zwischen 215 Patienten in der PCF- Gruppe und „nur“ 91 Patienten in der Subgruppenanalyse ist darauf zurückzuführen, dass die Datenübermittlung von externen Kliniken, an denen die Koronarangiographien erfolgten, unvollständig war. Wir schlossen die Patienten von der Studie aus, welche eine Koronarangiographie mit Intervention mehr als 3 Jahre vor der Bypassoperation hatten.

Die ESC/EACTS-Leitlinien von 2014 empfehlen eine PCI bei Patienten mit stabiler Ein- oder Zwei-Gefäß-KHK ohne proximale LAD-Stenose. Sollte eine Ein- oder Zweigefäß-KHK mit proximaler LAD-Stenose oder eine Hauptstammstenose vorliegen, der SYNTAX-Score aber <22 sein, sind eine CABG oder eine PCI gleichwertig anzusehen (Klasse I-Empfehlung). Patienten mit koronarer Dreigefäßerkrankung und einem SYNTAX-Score <22 ohne Diabetes mellitus werden ebenfalls beide Prozeduren (CABG oder PCI) mit einer Klasse I-Empfehlung angeboten. Die Patienten mit Hauptstammstenose, Diabetes mellitus und einem SYNTAX-Score >22 sollten sich einer koronaren Bypass-Chirurgie unterziehen (Dangas et al., 2014).

Patienten mit Nicht-ST-Hebungsinfarkt (NSTEMI) als auch Patienten mit ST-Hebungsinfarkt (STEMI) wurden von der Studie ausgeschlossen.

1.2.2 Prä- und postoperative Daten

Die Datensatzerhebung der prä-, intra- und postoperativen Patientendaten erfolgte durch Einsicht in das Krankenhaus-Informationssystem der Uniklinik Bonn (ORBIS KIS).

Hierüber konnten die kardiovaskulären Risikofaktoren (Vaskuläre Vorerkrankungen, Diabetes mellitus, arterielle Hypertonie, Hyperlipidämie) erhoben werden, ebenso wie die für das Outcome relevanten postoperativen Daten (Kontinuierliche veno-venöse Hämofiltration (CVVH), Beatmungsdauer, Intensiv- und Krankenhausliegedauer, 30-Tage-Mortalität) gesammelt werden.

Die in der Auswertung angegebenen „Scores" wurden aus den klinischen und demografischen Daten erhoben oder waren im Krankenhausinformationssystem bereits hinterlegt (STS-Score (Society of Thoracic Surgeons), EUROScore II (European System for Cardiac Operative Risk Evaluation II), SAPS II (Simplified Acute Physiology Score II) und TISS-10 (Therapeutic Intervention Scoring System)). Der SYNTAX-Score wurde mit Hilfe der verfügbaren Software (www.syntaxscore.com) und der vorliegenden Koronarangiographie berechnet.

1.2.3 Follow-up Daten

Die postoperativen Daten wurden telefonisch und postalisch erfasst. Zur Bewertung der Lebensqualität wurde der sogenannte EQ-5D-3L Fragebogen verwendet, ein standardisierter europäischer Fragebogen der EuroQoL-Gruppe mit fünf Dimensionen und drei Leveln, der die Erhebung der Lebensqualität ermöglicht (Rabin et al., 2001). Die fünf Dimensionen beinhalten Mobilität, Selbstversorgung, alltägliche Tätigkeiten, Schmerzen/Beschwerden und Ängste/Depressionen. Jede Dimension wird dann wiederum in drei Level unterteilt: keine Probleme, einige Probleme und extreme Probleme (EuroQol, 2023). Eine numerische Skala von 0-100 zur Darstellung des Gesundheitszustandes wurde verwendet, wobei „0" den schlechtesten und „100" den bestmöglichen Gesundheitszustand repräsentiert. Die Pflegebedürftigkeit der Patienten wurde über die fünf Pflegegrade (früher Pflegestufen) abgefragt. Des Weiteren wurde die Notwendigkeit einer Re-Angiographie, einer Re-Intervention mittels Stentimplantation, einer Schrittmacherimplantation oder einer erneuten Bypassoperation erhoben, sowie das Auftreten eines Schlaganfalls oder Myokardinfarktes postoperativ erfragt.

1.2.4 Statistik

Für die statistische Auswertung wurde mit IBM SPSS Statistik Version 25 (SPSS Inc., Chicago, IL, USA) gearbeitet. Während stetige Variablen als Mittelwert ± Standardabweichung (SD) angegeben wurden, wurden die kategorische Variablen als absolute Werte und Prozentsätze angegeben.

Nachdem mittels Kolmogorov-Smirnov- und Shapiro-Wilk-Test auf Normalverteilung geprüft wurde, konnten normalverteilte Daten mit dem zweiseitigen t-Test oder Mann-Whitney-U-Test analysiert werden. Für die kategorialen Variablen wurde der Chi-Quadrat-Test verwendet. Ein *p*-Wert von <0,05 wurde als statistisch signifikant angesehen.

Für die grafische Veranschaulichung der EQ-5D-Daten und deren Auswertung wurde die "EQ-5D"-Software (https://github.com/fragla/eq5d) genutzt.

1.3 Ergebnisse

1.3.1 Präoperative Daten

Es wurden präoperative Ausgangskriterien der Patienten aus den Hauptgruppen (PCF und CO) erhoben. Hier ergaben sich hinsichtlich der demografischen Daten, der Vorerkrankungen, der klinischen Symptomatik (NYHA, CCS), der Risikostratifizierung (EuroScore II, STS) und des präoperativen SYNTAX-Score keine Unterschiede.

In der Subgruppenanalyse konnte gemäß den ESC/EACTS-Leitlinien aus dem Jahr 2014 (Kolh et al., 2014) von 91 Patienten aus der PCF-Gruppe eine Unterteilung in 67 leitlinienkonform-behandelte Patienten (GCO: 73.6 %) und 24 nicht-leitlinienkonform-behandelte Patienten (GNC: 26.4 %) erfolgen (Hamiko, Konrad et al., 2023). Auch diese Untergruppen erhielten einen statistischen Vergleich in den selben präoperativen Ausgangskriterien wie die Hauptgruppen. Hier fiel auf, dass in der GNC-Gruppe signifikant häufiger Stenosen des Hauptstammes vorlagen (GNC: 37.5 % vs. GCO: 19.7 %; *p*<0.001) (Hamiko, Konrad et al., 2023). Ein ähnlicher Trend, jedoch ohne statistische Signifikanz, ließ sich bei der proximalen LAD-Stenose feststellen: Hier wiesen mehr als 80 % der nicht-leitlinienkonform-behandelten Patienten eine proximale LAD-Stenose auf (GNC: 83.3 % vs. GCO: 62.1 %; *p*=0.057) (Hamiko, Konrad et al., 2023).

Der SYNTAX-Score vor der Koronarintervention war - wie zu erwarten - in der GNC-Gruppe signifikant höher als in der GCO-Gruppe (GNC: 26.7 vs. GCO: 18.6; p=0.005) (Hamiko, Konrad et al., 2023). Vor der Bypass-Operation hingegen waren die SYNTAX-Scores wiederum vergleichbar. (GNC: 21.4 vs. GCO: 21.3; p=0.201) (Hamiko, Konrad et al., 2023).

1.3.2 Postoperative Daten

Hinsichtlich der Erstmobilisierung, der Wundheilungsstörungen, dem Auftreten eines postoperativen Delir, der Notwendigkeit einer vorübergehenden Hämodialyse (CVVH), einer Kreislaufunterstützung mittels ECMO (extracorporale Membranoxygenierung) oder IABP (intraaortale Ballonpumpe), der peri- und postoperativer Bluttransfusion (EK, TK, FFP), der Liegedauern (im Krankenhaus und auf der Intensivstation), der Beatmungsdauern konnten keine signifikanten Unterschiede zwischen den Haupt- und den Untergruppierungen festgestellt werden (Hamiko, Konrad et al., 2023). Auch die Risiko-Einstufung mittels SAPS-II und TISS-10 waren zwischen den Gruppen vergleichbar.

1.3.3 Nachbeobachtung und EQ-5D

Von den insgesamt 997 in der Zeit vom 01.01.2014 bis zum 31.12.2016 an der Universitätsklinik Bonn Bypass-operierten Patienten konnten 69 % Prozent der Patienten telefonisch oder postalisch erreicht werden. Dies geschah von 2017 bis 2018, sodass das Nachbeobachtungsintervall zwischen einem Jahr und viereinhalb Jahren betrug. Patienten ohne vorherige Stentimplantation gaben einen signifikant höheren/“besseren“ Gesundheitszustands (Skala 0-100) nach aortokoronarer Bypassoperation an (PCF: 68.2 vs. CO: 72.5; p=0.01). Im direkten Vergleich der Untergruppen der PCF-Patienten setzt sich der Trend fort, sodass die nicht-leitliniengerecht intervenierten Patienten ihren Gesundheitszustand signifikant schlechter bewerteten, als diejenigen die eine leitlinienkonforme Therapie erfahren hatten (GCO: 73.4 vs. GNC: 64.2; p=0.041) (Hamiko, Konrad et al., 2023).

In der PCF-Gruppe kam es signifikant häufiger zu postoperativen Myokardinfarkten (PCF: 3.8 % vs. CO: 1.0 %; *p*=0.024). Entsprechend wurden selbige Patienten auch häufiger re-koronarangiographiert (PCF: 17.6 % vs. CO: 9 %; *p*=0.004) und mittels Stentimplantation re-interveniert (PCF: 10.4 % vs. CO: 3 %; *p*<0.001) (Hamiko, Konrad et al., 2023).

In der Subgruppenanalyse konnte ergänzend gezeigt werden, dass die Patienten aus der GNC-Gruppe im Vergleich zu denen aus der GCO-Gruppe signifikant häufiger eine postoperative Stentimplantation benötigten (GCO: 2.4 % vs. GNC: 18.8 %; *p*=0.03) (Hamiko, Konrad et al., 2023).

Die Daten des EQ-5D-Fragebogens machten darüber hinaus deutlich, dass Patienten der PCF-Gruppe im Vergleich zur CO-Gruppe häufiger über eine eingeschränkte Mobilität berichteten, mehr Ängste/ Depressionen haben und häufiger über Schmerzen/ Beschwerden klagten. Dieser Trend war allerdings ohne statistische Signifikanz. Bei den Subgruppen zeigte sich Ähnliches für die GNC-Patienten im Vergleich zu den GCO-Patienten.

1.3.4 Datenanpassung nach aktuell geltenden Leitlinien

Die Daten wurde zusätzlich am aktuellen Maßstab der geltenden ESC-Leitlinien von 2018 (Neumann et al., 2019) gemessen, um die Aktualität der Daten zu belegen: In der GNC-Gruppe war der Syntax-Score im Vergleich zur GCO-Gruppe signifikant höher (GCO: 18.7 vs. GNC: 24.4; *p*=0.007). Ebenso war die Hauptstammstenose in der GNC-Gruppe signifikant häufiger (GCO: 17.5 % vs. GNC: 54.5 %; *p*<0.001). Eine erneute Angiografie nach Bypasschirurgie war in der GNC- im Vergleich zur GCO-Gruppe signifikant häufiger zu beobachten.

1.4 Diskussion

Die Eignung von einer perkutanen Koronarintervention versus einer aortokoronaren Bypasschirurgie wurde bereits in einigen Studien im Hinblick auf das sogenannte Outcome verglichen (Deb et al., 2013).

Die letzten Jahre und Jahrzehnte haben gezeigt, dass die Behandlung komplexer KHK-Patienten nicht mehr allein der Kardiochirurgie zufällt, sondern mehr und mehr komplexe perkutane Koronarinterventionen durch die Kardiologie erfolgen. Aufgrund der günstigen Ergebnisse der Fünfjahresdaten nach PCI hat sich diese Methode für die meisten Indikationen als Goldstandard durchgesetzt (Serruys et al., 2009). Zur Entscheidungsfindung für diese oder jene Revaskularisationsstrategie wurde eine verbindliche Leitlinie erarbeitet, welche sich in den ESC-Leitlinie wiederfindet und in Form des SYNTAX-Scores einen Wert als Anhalt für die therapeutische Strategie festlegt. Mit dem SYNTAX-Score ist die Bestimmung der Komplexität einer KHK unter Berücksichtigung der Anzahl der erkrankten Gefäße möglich. Die ESC und die EACTS haben ihn daher übernommen und als Entscheidungshilfe (PCI versus CABG) popularisiert (Neumann et al., 2019).

Die Zunahme der komplexen PCI führt, auch vor dem Hintergrund, dass oftmals eine PCI bei eigentlich für CABG infrage kommender Patienten durchgeführt wird, zu weniger operativen Revaskularisierungen. Dies ist laut aktuellen Studien mit einer höheren Morbidität und Mortalität verbunden (Frutkin et al., 2009; Head et al., 2013).

Dennoch führt der Umstand, dass die PCI als weniger invasive Revaskularisierungsstrategie attraktiver beurteilt wird, unabhängig vom SYNTAX-Score, zu einer PCI auch bei einer 3-Gefäß-KHK. Die Missachtung der Leitlinie wird durch die Tatsache unterstrichen, dass bis zu 1/3 der Ad-hoc-PCI-Patienten aufgrund ihrer koronaren Befunde Kandidaten für eine CABG wären (Hannan et al., 2009). Dies führt zu einer Veränderung des Patientengutes, welches der CABG zugeführt wird: Die CABG-Patienten sind älter, weisen mehr Komorbiditäten auf und haben bei oftmals vorangegangene Koronarintervention mit hierdurch auch anatomisch komplexere Läsionen, die es dann zu operieren gilt (Frutkin et al., 2009). Infolgedessen weisen bis zu 1/3 der Patienten, die zur Bypassoperation vorgestellt werden, eine vorangegangene PCI auf (10-30 %) (O'Brien et al., 2018). Diese Daten sind im Einklang mit unserer Studie, in welcher 21 % der Patienten vor CABG eine PCI erhielten (Hamiko, Konrad et al., 2023).

In diversen Studien wurde bereits die Thematik der Morbidität und Mortalität für Patienten nach Bypassoperation analysiert. Als Ergebnis zeigte sich, dass eine vorangegangene

Koronarintervention ein unabhängiger Risikofaktor für die Krankenhaussterblichkeit nach CABG war und das unabhängig davon, welche Gefäße als Bypass-Grafts verwendet wurden (Lisboa et al., 2012). Mehrfache Koronarinterventionen steigerten sogar die Krankenhaussterblichkeit. Außerdem traten bei diesen Patienten schwerwiegendere, unerwünschte kardiale und zerebrovaskuläre Ereignisse nach CABG auf (Massoudy et al., 2009). Diese Studienergebnisse konnten wir allerdings nicht bestätigen, da sich in unserem Datensatz bei Patienten, die sich einer Koronarintervention bis zu drei Jahre vor der Bypassoperation unterzogen hatte, kein Unterschied im Überleben ergab (Hamiko, Konrad et al., 2023). Auch andere Studien bekräftigten dies (Gaszewska-Zurek et al., 2009; Boening et al., 2011; Mannacio et al., 2012).

Eine Studie aus Virginia von 2012 zeigt auf, dass Patienten mit vorangegangener Koronarintervention eine höhere Inzidenz postoperativer unerwünschter Ereignisse, eine längere Krankenhausverweildauer und sogar höhere Rückübernahmeraten nach CABG aufwiesen (Mehta et al., 2012). In unserer Analyse konnten weder Unterschiede im Auftreten von postoperativem Nierenversagen mit der Notwendigkeit einer CVVH, noch in der Notwendigkeit einer linksventrikulären Unterstützung (ECMO, IABP), noch in der Transfusion von Blutprodukten, noch bei Wundheilungsstörungen oder Delirium festgestellt werden (Hamiko, Konrad et al., 2023). Ein postoperativer Myokardinfarkt, eine erneute Koronarangiographie und auch Re-Interventionen mit Stent-Implantation nach CABG konnten hingegen häufiger in der PCI-Gruppe gesehen werden (Hamiko, Konrad et al., 2023). Diese Ergebnisse decken sich mit vorherigen Studienergebnissen (Miguel et al., 2020). Im Hinblick auf die aktuell gültigen ESC/EACTS-Leitlinien von 2018 war auch die Re-angiographie in der GNC-Gruppe signifikant häufiger als in der GCO-Gruppe (Hamiko, Konrad et al., 2023).

Das SYNTAX-Klassifikationssystem wurde in der Vergangenheit angeprangert, nicht geeignet zu sein, die frühe Sterblichkeit bei PCI-Patienten, die zur CABG eingewiesen werden, vorherzusagen (Bonaros et al., 2011). Der SYNTAX-Score ist ein empfindliches Klassifikationsinstrument, welches die Komplexität der Koronaranatomie widerspiegelt und welches daher auch von den medizinischen Fachgesellschaften zur Therapieempfehlung herangezogen wird. Unsere Daten zeigen vergleichbare SYNTAX-Scores in den Gruppen PCF und CO vor der CABG (Hamiko, Konrad et al., 2023). Im

Kontrast dazu stehen die Untergruppierungen: Patienten, die entgegen den genannten Leitlinien mit einer Koronarintervention behandelt wurden (GNC-Gruppe), wiesen folglich einen signifikant erhöhten präinterventionellen SYNTAX-Score auf (Hamiko, Konrad et al., 2023). Eben selbe Patienten hatten signifikant häufiger Hauptstammstenosen im Vergleich zu denen, die mit einer leitliniengerechten CABG behandelt wurden (GCO-Gruppe) (Hamiko, Konrad et al., 2023). Eine nicht-leitlinienkonforme Koronarintervention war zudem mit einer signifikant höheren Inzidenz einer nachfolgenden Stentimplantation nach Bypassoperation vergesellschaftet (Hamiko, Konrad et al., 2023).

Wie oben bereits erwähnt, ergab sich erfreulicherweise in unserer Studie kein Unterschied in der Mortalität. Was aber in vorherigen Studien noch nicht berücksichtigt wurde, ist das subjektive Wohlbefinden der Patienten. Wir betrachteten daher die Lebensqualität in einer postoperativen Analyse mittels EQ-5D-Fragebogen (EuroQol Group, 1990). Wir konnten zeigen, dass die Patienten, die vor der CABG koronarinterveniert wurden, einen schlechteren Gesundheitszustand angaben als Patienten, die sich nur einer CABG unterzogen (Hamiko, Konrad et al., 2023). Warum sollte die vorherige Koronarintervention zu einem schlechteren postoperativen Ergebnis führen? Hier kommen mehrere Faktoren zusammen: Zum einen muss bedacht werden, dass Stents zu einer lokalen Entzündung in der Gefäßwand führen, welches mit einer endothelialen Dysfunktion einhergeht (Massoudy et al., 2009; Lisboa et al., 2012). Zum anderen stellen Koronarstents eine technische Herausforderung in der Operation dar hinsichtlich der Möglichkeit zur Anastomisierung. Gefäß-Grafts müssen weiter distal im Gefäßsystem angeschlossen werden, was möglicherweise mit einem schlechteren Blutfluss durch das Graft verbunden ist (Kamiya et al., 2004). Entsprechend zeigten die Fünfjahresdaten nach Koronarintervention eine notwendigen erneute Revaskularisierung von 25,9 % (Stolker et al., 2012). Bei uns waren es aus der PCF-Gruppe 17,6 % der Patienten, die sich einer erneuten Koronarangiographie postoperativ unterziehen mussten. 10,4 % benötigten dann auch eine erneute Koronarintervention (Hamiko, Konrad et al., 2023). Im Hinblick auf die Untergruppierung gemäß der ESC/EACTS-Leitlinien waren die Ergebnisse noch brisanter: Nicht-leitlinienkonform behandelte Patienten wurden mehr als doppelt so häufig erneut koronarangiographiert (11,6 % Re-Angiographie in der GCO-Gruppe versus 29,4 % Re-Angiographie in der GNC-Gruppe), und der Anteil für eine erneute

Koronarintervention stieg von 2,4 % (GCO) auf 18,8 % (GNC) (Hamiko, Konrad et al., 2023). In der Angabe der Lebensqualität mittels EQ5D-Fragebogen ergänzen sich die Ergebnisse, da eine erneute Stentimplantation nicht nur mit einer Verschlechterung des subjektiven Gesundheitszustandes einherging, sondern auch weitere Dimensionen der Lebensqualität betroffen waren: Angst oder auch Mobilität waren reduziert, während die Selbstversorgung und tägliche Aktivitäten entlastet wurden, wenn die Koronarintervention leitlinienkonform erfolgte (Hamiko, Konrad et al., 2023). Es ergänzt sich passend hierzu, dass in einer Studie aus dem New England Journal of Medicine 2011 Patienten mit komplexer koronarer Herzkrankheit nach CABG ihre Angina pectoris Beschwerden als stärker gelindert ansahen als nach einer Koronarintervention (Cohen et al., 2011).

In der Zusammenschau ist es daher nicht verwunderlich, dass Patienten, die gemäß den gültigen ESC/EACTS-Leitlinien chirurgisch revaskularisiert werden sollten, klinisch von der operativen Versorgung profitieren (Hamiko, Konrad et al., 2023). Die Ergebnisse dieser Studie heben noch einmal hervor, wie wichtig die gemeinsame Herangehensweise mittels Herzteam sowie die Einhaltung der anerkannten Leitlinien bei der Findung der „richtigen“ Revaskularisierungsstrategie für den individuellen Patienten sind (Hamiko, Konrad et al., 2023).

1.5 Zusammenfassung

Eine perkutane Koronarintervention vor koronarer Bypasschirurgie hat keinen direkten Einfluss auf das Überleben der Patienten. Patienten mit präoperativer PCI gaben einen schlechteren Gesundheitszustand im EQ-5D-Fragebogen an. Zu beobachten war außerdem, dass Patienten mit präoperativer PCI häufiger postoperativ Myokardinfarkte erlitten, sowie re-koronarangiographiert und dann auch re-interveniert werden mussten. Patienten, die zudem eine leitlinienkonformen PCI erfahren hatten vor CABG, gaben eine bessere Lebensqualität an und wurden signifikant seltener re-koronarinterveniert. Die Wichtigkeit der leitliniengerechten Therapie und vor allem die Bedeutung der Entscheidung zur Revaskularisierungsstrategie in einer gemeinsamen Herzkonferenz wird durch diese Dissertationsarbeit deutlich.

1.6 Einschränkungen

Die Dissertation weißt einige Limitationen auf.

Es handelt sich zum einen um eine retrospektive Studie eines einzigen Zentrums. Zum anderen haben wir aufgrund des Zeitraums, in dem die Patienten in diese Studie eingeschlossen wurden, die ESC/EACTS-Leitlinien von 2014 für die Bewertung der Leitlinieneinhaltung verwendet.

Auf die ursprünglich geplante Regressionsanalyse für die primären Endpunkte musste angesichts ähnlicher Kurzzeitergebnisse zwischen den Gruppen sowie der geringen Stichprobengröße der Untergruppen verzichtet werden. Es fehlt zudem, aufgrund zu geringer Stichprobengröße, der direkte Vergleich zwischen Patienten ohne vorherige PCI und solchen mit einem oder mehreren vorherigen PCI.

Nur eine geringe Anzahl von Patienten war aus der GNC-Gruppe im Follow-up zu erreichen, sodass bei folglich wenig beantworteter EQ-5D-Fragebögen die Aussagekraft der Ergebnisse beeinträchtigt wird.

Das retrospektive Studiendesign weist die bekannten Einschränkungen auf (Anfälligkeit für Selektions- und Beobachtungsfehler; Unmöglichkeit, Patienten aus strukturellen oder krankenversicherungsrechtlichen Gründen erneut zu sehen), weshalb unsere Daten durch prospektive Studien, Register-Studien oder Meta-Analysen bestätigt werden sollten.

1.7 Literaturverzeichnis der deutschen Zusammenfassung

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Follow-up and outcome after coronary bypass surgery preceded by coronary stent implantation

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Abstract:
Background: Guidelines on myocardial revascularization define recommendations for percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery. Only little information exists on long-term follow-up and quality of life (QoL) after CABG preceded by PCI. The aim of our study was to evaluate the impact of prior PCI on outcome and QoL in patients with stable CAD who underwent CABG.
Methods: In our retrospective study, 997 CABG-patients were divided in: CABG preceded by PCI: PCI-First (PCF)-, and CABG-only (CO)-groups. The PCF-group was further divided in guideline-conform (GCO) and guideline non-conform (GNC) sub-groups, according to the SYNTAX-Score (2014 ESC-guidelines). Thirty-days mortality, major adverse cardiac events and quality-of-life using EQ-5D were evaluated.
Results: Re-infarction (PCF: 3.8% vs. CO: 1.0%; p=0.024), re-angiography (PCF: 17.6% vs. CO: 9.0%; p=0.004), and re-PCI (PCF: 10.4% vs. CO: 3.0%; p<0.001) were observed more frequently in PCF-patients. Also, patients reported better health-status in the CO- compared to PCF-group (CO: 72.48±19.31 vs. PCF: 68.20±17.86; p=0.01). Patients from the guideline non-conform sub-group reported poorer health-status compared to guideline-conform group (GNC: 64.23±14.56 vs. GCO: 73.42±17.66; p=0.041) and were more likely to require re-PCI (GNC: 18.8% vs. GCO: 2.4%; p=0.03). Also, GNC-patients were more likely to have left main stenosis (GCO: 19.7% vs. GNC: 37.5%; p<0.001) and showed higher pre-interventional SYNTAX-Score (GCO: 18.63±9.81 vs. GNC: 26.67±5.07; p<0.001).
Conclusion: PCI preceding CABG is associated with worse health-status and higher re-hospitalization. Nevertheless, results were better when PCI was guideline-conformant. This data should impact the Heart-Team decision.

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Follow-up and outcome after coronary bypass surgery preceded by coronary stent implantation

Abstract

Background: Guidelines on myocardial revascularization define recommendations for percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery. Only little information exists on long-term follow-up and quality of life (QoL) after CABG preceded by PCI. The aim of our study was to evaluate the impact of prior PCI on outcome and QoL in patients with stable CAD who underwent CABG.

Methods: In our retrospective study, CABG-patients were divided in: CABG preceded by PCI: PCI-First (PCF)-, and CABG-only (CO)-groups. The PCF-group was further divided in guideline-conform (GCO) and guideline non-conform (GNC) sub-groups, according to the SYNTAX-Score (2014 ESC/EACTS-guidelines). Thirty-days mortality, major adverse cardiac events and quality-of-life using EQ-5D were evaluated.

Results: A total of 997 patients were analyzed, of which 784 underwent CABG without (CO), and 213 individuals with prior PCI (PCF). The latter group consisted of 67 patients being treated in accordance (GCO), and 24 in discordance GNC) to the 2014 ESC/EACTS-guidelines. Re-infarction (PCF: 3.8% vs. CO: 1.0%; p=0.024), re-angiography (PCF: 17.6% vs. CO: 9.0%; p=0.004), and re-PCI (PCF: 10.4% vs. CO: 3.0%; p<0.001) were observed more frequently in PCF-patients. Also, patients reported better health-status in the CO- compared to PCF-group (CO: 72.48±19.31 vs. PCF: 68.20±17.86; p=0.01). Patients from the guideline non-conform subgroup reported poorer health-status compared to guideline-conform group (GNC: 64.23±14.56 vs. GCO: 73.42±17.66; p=0.041) and were more likely to require re-PCI (GNC: 18.8% vs. GCO: 2.4%; p=0.03). Also, GNC-patients were more likely to have left main stenosis (GCO: 19.7% vs. GNC: 37.5%; p<0.001) and showed higher pre-interventional SYNTAX-Score (GCO: 18.63±9.81 vs. GNC: 26.67±5.07; p<0.001).

Conclusion: PCI preceding CABG is associated with poorer outcomes such as re-infarction, re-angiography and re-PCI, but also worse health-status and higher re-hospitalization. Nevertheless, results were better when PCI was guideline-conformant. This data should impact the Heart-Team decision.

Key words

Coronary artery bypass graft surgery

Percutaneous coronary intervention

Quality of life

Introduction

Among cardiovascular diseases, coronary artery disease (CAD) is one of the most relevant causes for mortality and morbidity in all countries.[1-3] Standard therapy is revascularization, associated with hospitalization, high treatment costs and often restricted long-term outcome.[1, 2] The concept of early revascularization led to improved long-term outcome in patients with CAD. The European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed guidelines on myocardial revascularization: According to the guidelines, different strategies are recommended, e.g. percutaneous coronary intervention (PCI), or coronary artery bypass graft surgery (CABG).[4, 5] Over the last years, the SYNTAX-Score (SYNergy between PCI with TAXus and Cardiac Surgery) has become an important instrument for decision-making with respect to therapeutic regime.[3-11] During the last decades, primary PCI was established as the predominant therapy, and CABG is reserved for extensive disease and high complexity of coronary anatomy.[5] Nevertheless, due to extensive research on stent material as well as comparable five-years results of PCI and CABG in complex coronary anatomy, indications were increasingly made in favor of PCI.[12-15] Recently, multivessel PCI is getting more and more popular, not just in low-risk, but also in high-risk patients affected by complex CAD, including left main stenosis, or patients with diabetes mellitus.[16] For the CABG option, this results in an increasing number of patients with previous PCI and rising complexity of coronary lesions, making CABG more difficult.[17, 18] Of note, 10-30 % of patients presenting for CABG underwent previous PCI.[19, 20]

Therefore, we hypothesize that this patient cohort is at risk, as repeated PCI procedures might postpone complete revascularization, thus leading to re-hospitalization.[21] Importantly, previous PCI is recognized as a perioperative risk factor for CABG[18, 19] Several studies attempted to analyze early and late outcomes in this patient population, but the prognostic impact of prior PCI in patients requiring CABG remains elusive.[22] Therefore, the aim of our study was to evaluate the outcome of CABG patients with or without preceded PCI, especially in the light of ESC/EACTS-guideline conform and guideline non-conform PCI.

Material and Methods

Patients

In this retrospective study, we evaluated data of 997 consecutive patients who underwent isolated CABG in a major heart center in Germany. A signed patient permission form was obtained from every patient. CABG surgery and postoperative treatment was performed as described before.[23] According to preceded PCI and stent therapy we classified patients in two groups: (PCI-First, PCF)-patients with previous PCI within 3 years before CABG (n=213) and (CABG-only, CO)-patients without previous PCI (n=784). The PCF-group was further divided in patients where PCI was in accordance to the ESC/EACTS-guidelines (guideline compliant, GCO, n=67) and patients that received guideline non-conform PCI (GNC, n=24); Subgroup-analysis for GCO- and GNC-groups was performed in only 91 of the total 213 patients from the

PCF-population due to incomplete data transfer from external catheterization clinics. The PRISMA diagrams in ***Figures 1 and 2*** summarize the design and patient number in the present study. According to 2014 ESC/EACTS-guidelines, PCI is recommended in one-vessel CAD; Patients with stable one- or two- vessel CAD with proximal left descending artery (LAD) stenosis or with/without a left main stenosis (LM) and a SYNTAX Score <22 could undergo CABG or PCI. Patients with stable three-vessel CAD and a SYNTAX Score <22 without diabetes mellitus are recommended for PCI or CABG. All patients including LM stenosis, diabetes mellitus and a SYNTAX-Score >22 should be treated with CABG.[5, 24]

Due to complexity of the study design, patients with non ST-segment elevation myocardial infarction (NSTEMI) as well as STEMI were excluded from the study.

A comprehensive data set of pre-, intra- and postoperative parameters was generated by review of the patient charts and IT based data sets. Clinical and demographic data, medical history, including cardiovascular risk factors, former cerebrovascular disease, and preoperative risk score systems like the STS-Score (Society of Thoracic Surgeons), EUROScore II (European System for Cardiac Operative Risk Evaluation II) and the SYNTAX-Score were recorded.

Preoperative patient characteristics

Demographic characteristics, preexisting medical conditions (e.g. diabetes mellitus, cerebral artery disease, history of stroke, arterial hypertension, hyperlipidemia) were collected directly from the patient or indirectly from the hospital information system (ORBIS), and clinical predictive scores (EUROScore II and STS-score) were calculated. The SYNTAX-Score was calculated using the available software *(www.syntaxscore.com)* and the respective coronary angiogram.[9-11] Clinical presentation was documented using the New York Heart Association (NYHA)- and the Canadian Cardiovascular Society (CCS)-classification.

Postoperative outcome

Outcome data included: renal failure with need for continuous veno-venous hemofiltration or -dialysis (CVVH/HD), ventilation time, length of ICU and hospital stay, nurse workload score (Therapeutic Intervention Scoring System [TISS]-10) and monitoring of the Simplified Acute Physiology-ScoreII (SAPSII), as well as 30-days mortality.

Follow-up data

Follow-up data was collected via telephone or mail. The standard European Quality-of-Life–5 Dimensions and 3 Levels (EQ-5D-3L) health questionnaire was used for evaluation of quality-of-life. Accordingly, a scale from 0-100 represented the state of health, zero points indicating worst, and 100 points best health status. The need for care was queried via the care levels (1-5) applicable in Germany. We further evaluated the need for post-operative re-angiograms as well as re-PCI or re-CABG.

Statistical analysis

Statistical analysis was performed using the IBM SPSS statistics version 25 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were given as absolute values and percentages. Data were tested for normal distribution using Kolmogorov-Smirnov and

Shapiro-Wilk tests. Normally distributed data were analyzed using the two-tailed students t-test or Mann–Whitney U-test where appropriate. For categorial variables Pearson chi-square-test was used. A *p*-value of <0.05 was considered statistically significant. For graphical display of EQ-5D evaluation results were created using the "EQ-5D"-software (*https://github.com/fragla/eq5d*).

Results

Preoperative patients' characteristics and preoperative risk-stratification

Patients' baseline characteristics are displayed in ***Tables 1 and 2***: No differences were observed with respect to demographic data, prevalence of pre-existing disease, surgery risk stratification as well as SYNTAX-Score in the PCF- and CO-groups.

Out of the PCF-patients, 67 were treated according to the 2014 ESC/EACTS-guidelines for myocardial revascularization [5] (GCO: 73.6%), while in 24 patients that received a PCI prior to CABG guidelines would have recommended primary CABG and were therefore not treated according to current guidelines (GNC: 26.4%). In the latter, left main (LM) stenosis occurred more often (GNC: 37.5% vs. GCO: 19.7%; *p*<0.001), as shown in ***Table 2***. Also, more than 80% of GNC-group demonstrated with a proximal LAD stenosis (83.3% vs. GCO: 62.1%; *p*=0.057). While the SYNTAX-Score before PCI was higher in GNC-group (26.7 vs. GCO: 18.6; *p*<0.001), the SYNTAX-Score before subsequent CABG was comparable between the groups (GNC: 21.4 vs. GCO: 21.3; *p*<0.201).

Postoperative outcome

In ***Table 3 and 4***, postoperative patients' data are displayed: no significant differences are observed with respect to the length of ICU- or total hospital stay, ventilation time, ICU risk-and nurse workload index-scores (SAPSII and TISS-10), postoperative complication with the need for CVVH, mechanical circulatory support (ECMO or intra-aortic balloon pump, IABP), perioperative blood transfusions, delirium, and wound healing disorder. Also, the 30-days mortality as well as long-term survival was comparable in both compared scenarios, CO vs. PCF and PCF-subgroups GCO vs. GNC (***Figures 3A and B***). In the PCF-group, outcome between 1- or 2-vessel CAD vs. 3-vessel CAD was examined: (***Supplementary Table 3S)*** shows longer ventilation time in 1-/2-vessel disease, but higher need for platelet transfusions in 3-vessel disease.

Follow-up and EQ-5D

Postoperative follow-up period was between one to 4.5 years. Sixty-nine percent of the patients could be contacted, and 63.3% answered to the EQ-5D questionnaire. The EQ-5D score for evaluation of the state of health after CABG was significantly higher in patients without previous PCI/stent implantation (PCF: 68.20 vs. CO: 72.48; p=0.01; ***Table 5***). Compared to CO-group, PCF-group had a higher incidence of postoperative myocardial infarctions (PCF: 3.8% vs. CO: 1.0%; p=0.024). Accordingly, the rate of coronary re-angiography (PCF: 17.6% vs. CO: 9%; p=0.004) and the need of repeated stent implantation (10.4% vs. 3%; p<0.001) were significantly higher in this group. The latter was also true for patients of GNC- compared to GCO-group (GCO: 2.4% vs. GNC: 18.8%; p=0.03; ***Table 6***). Also, the postoperative state of health in GNC-patients was significantly lower than in GCO-group (GCO:73.42 vs. GNC: 64.23 p=0.041; ***Table 6***). The radar diagram in ***Figure 4A*** reflects the data from EQ-5D questionnaire and indicate that patients in the PCF group more often reported reduced mobility, anxiety/depression, and pain/discomfort compared to the CO group; The same was seen when in GNC compared to GCO group ***(Figure 4B).*** On the other hand, GCO patients reported better ability with respect to usual activities self-care.

So that our data can be evaluated against current standards with respect to the 2018 ESC/EACTS-guidelines, [4] we ran the same analysis based on these current guidelines (***Supplementary Tables 2S and 4S***), confirming that re-angiography was significantly more frequent in GNC- compared to GCO-group.

Discussion

Several studies compared the efficacy of PCI and CABG with respect to the outcome.[25, 26] Comparable five years results between PCI and CABG in multivessel coronary lesions have inaugurated the PCI therapy as an equal therapy over the last decades.[6] Therefore, PCI gained acceptance for treatment of CAD also with complex lesions. As a consequence, PCI lead to less CABG, but was also associated with higher morbidity and mortality.[5, 17, 18]

Therefore, the SYNTAX score has been established to predict the postprocedural risk associated with PCI or CABG. The SYNTAX score is an angiographic tool that determines the complexity of CAD, taking into account the number of diseased vessels. It was derived from pre-existing risk assessment classifications from numerous studies and expert consensus; Medical cardiovascular and cardiothoracic societies such as the ESC/EACTS adopted it and further propagated it as decision making tool in order facilitate the decision in favor to PCI or CABG.[4, 5]

Nevertheless, as PCI is recognized as less invasive therapy for revascularization of CAD by many interventionalists, PCI is favored over CABG irrespective of SYNTAX-score, sometimes also engaging 3-vessel CAD. For this reason, interventionalists sometimes do not adhere to the existing guidelines, which is underlined by the fact that up to 30% of ad hoc PCI patients would have been candidates for CABG due to their coronary findings.[27]

In return, as PCI has become commonly available, the profile of patients subjected to CABG also changed: As a result, CABG patients now present with more comorbidities, are older and many of them underwent prior PCI, resulting in anatomically more complex lesions for CABG surgery.[17, 18] For this reason, cardiac surgeons often face patients referred to CABG with prior PCI therapy. The number of patients with prior PCI is reported to be about 10-30%.[20] In our study, 21% of the patients who presented for CABG had a history for preceding PCI.

Guidelines such as the ESC/EACTS guideline on myocardial revascularization make a recommendation for the therapeutic strategy for patients with CAD according to their coronary anatomy and complexity of lesions, e.g. PCI or CABG.[5] One of the aims of our study was to evaluate patients' outcome after undergoing different strategies for revascularization.

Different studies analyzed the long-term morbidity and mortality for this group, revealing prior PCI as an independent risk factor for in-hospital mortality after CABG, irrespective of which vessels where used as bypass grafts.[15, 19] Also, previous multiple PCI was associated with higher in-hospital mortality and major adverse cardiac and cerebrovascular events after CABG.[14, 28] In contrast, our work could show that CABG preceded by PCI within 3 years did not influence survival. Other studies confirmed our findings.[29-32] Recently, a retrospective single center study including 11,332 CABG patients showed that prior PCI had no impact on 5-, 10- and 15-year survival when comparing them to CABG patients without prior PCI.[33] A prospective multicenter registry investigated the prognostic impact of multiple prior PCI in CABG patients and showed an adjusted 30-day mortality rate of 1.3% to 3.1%, depending on the number of vessels that were intervened before CABG.[34] Of note, our data showed no differences in mortality and outcome with respect to the number of bypass-grafts implanted in patients with prior PCI.

However, Mehta et al. showed that PCI patients had higher incidence of postoperative adverse events, longer hospitalization time and higher readmission rates after CABG.[29] Our data could not show any difference with respect to the incidence of renal failure with need for CVVH, need for left ventricular assist (EMCO, IABP), transfusion of blood products and wound healing disorder or delirium. Also, ICU-related risk score SAPS-II and nurse workload index TISS-10 were similar.

On the other hand, we could demonstrate that PCI resulted in a significantly higher incidence for MI, Re-PCI and re-angiography after CABG. When current 2018 ESC/EACTS-guidelines were applied, re-angiography was also significantly more frequent in GNC- compared to GCO-group. Although the incidence for MI and Re-PCI were not significantly different under these circumstances, the time of patient inclusion to this study has to be considered. This data is in accordance with previous studies, which confirms negative influence of PCI in cardiovascular readmission rate at 5-year follow-up after CABG.[22] In this regard, it is important to point out that preoperative risk assessment scores EuroSCORE II and the STS-Score have been comparable in patients of all examined groups in our study, e.g. CABG only (CO), PCI-first (PCF), and even subgroups, e.g. guideline-conformant PCI (GCO) and guideline-nonconformant (GNC) groups.

Of note, it has been reported that the aforementioned scoring systems are not accurate to predict early mortality in PCI patients admitted for CABG.[35] As described above, a sensitive scoring system to predict the postprocedural risk associated with PCI or CABG is the SYNTAX scoring system. It describes the complexity of the coronary anatomy and medical societies such as ECS/EACTS take advantage of it for their recommendation for treatment of CAD. Our data reveals comparable SYNTAX score before CABG in both, patients undergoing CABG with (PCF) and without (CO) prior PCI. In contrast, we could demonstrate significantly enhanced pre-interventional SYNTAX score in patients that were treated with PCI in disagreement with the above-mentioned guidelines (GNC group). Not surprisingly, these patients also showed a significantly higher incidence of left main (LM) stenosis compared to those treated with CABG in accordance with the guidelines (GCO group). Of note, according to the ESC/EACTS-guidelines, CABG should be performed in patients with multivessel disease, LM stenosis and complex CAD.[4, 5] Furthermore, not guideline-conformant PCI was associated with significantly higher incidence of subsequent stent implantation after CABG.

Our data buttresses the impression that patients with prior PCI reveal a higher incidence of complications such as MI, Re-angiography and Re-PCI after CABG. This data is in accordance with previous studies.[22] Whereas survival is fortunately not affected, previous studies do not give consideration to the subjective well-being of these patients. Therefore, our study particularly evaluated quality of life of these patients using the EQ-5D questionaire.[36] We could show that higher incidence of MI, re-angiography and stent implantation was associated with lower state of health in patients that received PCI before CABG, which was significantly better in in patients who underwent CABG only.

There are multiple reasons why prior PCI might cause a deteriorated outcome after CABG. On one side, the presence of coronary stents increases the technical difficulty of surgery, including limitations with respect to the number of anastomoses and grafts to be anastomosed to more distal landing zones, possibly resulting in a worse graft patency.[37] Furthermore, stents cause a local inflammatory reaction in the coronary vessels' wall resulting in endothelial dysfunction[4, 19, 28]. It therefore seems logic that these changes complicate the outcome and are associated with higher need of re-interventions, as demonstrated by the five-year results of the SYNTAX trial with a reported rate of repeat revascularization after PCI of 25.9%.[38] This was further corroborated by a large registry study.[39] Hence, these studies underpin our data, showing 17.6% of patients needing re-angiography and 10.4% re-PCI when CABG was preceded by PCI.

Furthermore, we shed light on patients where CABG was performed within 3 years after PCI, with particular attention to those patients where PCI was not according to the recommendations of the ESC/EATCS guidelines. As to these patients, the above-mentioned results were even more striking: When PCI was not performed in accordance with the guidelines, the incidence for re-angiography doubled from 11.6% to 29.4% when compared to patients with guideline-conformant PCI, and went up to18.8% for re-PCI compared to 2.4%. To our knowledge, this is the first study that sheds light on an unexpressed problem of misguided therapeutic strategy for CAD treatment.

Keeping in mind the quality of life of these patients, it seems obvious that significantly enhanced incidence for re-stent implantation goes along with deteriorated subjective state of health, as revealed by the EQ-5D. Also, specific qualities of quality of life, e.g. anxiety, mobility, and discomfort, are reduced while self-care and usual activities are unburdened when PCI was done in accordance with the guidelines. Being in line with this, Cohen et al. compared quality of life of patients that underwent CABG or PCI: Among patients with three-vessel or LM coronary artery disease, there was greater relief from angina after CABG than after PCI after 6 and 12 months.[40] In this light, our data appears plausible as patients eligible for surgical revascularization according to the ESC/EACTS guidelines benefit from a CABG-only strategy.

The present study emphasizes the importance of the heart team approach and adherence to acknowledged guidelines. This is especially true when complete interventional treatment of CAD is not feasible and/or if later treatment has to be anticipated.

Conclusion

PCI preceding CABG does not influence survival, but the outcome is more often impaired by MI, re-angiography and re-PCI. This was further associated with worse health status revealed by EQ-5D quality of life questionnaires. In addition, patients that have undergone guideline conformant CABG-preceding PCI reported a better quality of life and could be spared additional invasive and expensive interventions. Therefore, the present study emphasizes the importance of the heart team approach for coronary revascularization.

Limitations

This study is a single-center retrospective study. The retrospective design increases susceptibility to selection and observational bias. Further, we used the 2014 ECS/EACTS guidelines for evaluation of guideline-compliance due to the time period during which the patients were included in this study.

With respect to statistical limitations, the originally planned regression analysis for the primary endpoints was abandoned in light of similar short-term outcomes between the PCF and CO groups as demonstrated in ***Tables 3 and 4*** as well as small sample size in the GCO and GNC subgroups. Also, due to small sample size, our study lacks direct comparison of patients without previous PCI and those with one, two or multiple previous PCI procedures. Small sample size in PCF-subgroups further foiled propensity score matching.

Finally, we have only a small number of patients from the GNC group that provided EQ-5D questionnaires, reducing the robustness of the results. The inability to see patients again due to structural or health insurance reasons is a general restriction that applies to most retrospective studies. Therefore, our data has to be confirmed by prospective studies, registries or meta-analysis.

Authors' Contributions

Conceptualization: GDD, MH, CG. Methodology: GDD, MH, NK, FM, CG. Software: MH, NK, DL, CG, FM. Validation: NK, MH, FM, CG. Formal analysis: GDD, MH, NK. Investigation: GDD, MH, NK. Resources: GDD, NK, DL: Data curation: MH, NK, DL, GDD. Writing – original draft preparation: MH, NK, GDD.

Writing – review and editing: GDD, CG, MO, MV, HT. visualization: GDD, MH, FM, MO, MV, HT: Supervision: GDD, MH. Project administration: GDD, MH.

Marwan Hamiko and Nicole Konrad contributed equally to this paper.

Conflict of Interest

All authors confirm that they have no conflict of interests.

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Figure 1: This PRISMA diagram summarizes the design and patient number in the present retrospective study.

Figure 2: The PRISMA diagram provides data on the feedback from patients in the different study subgroups

Figure 3: The Kaplan-Meier curves demonstrate similar survival between **(A)** CABG-only (CO) and PCI-first (PCF) as well as PCF-subgroups **(B)** guideline-conform (GCO)- and non-conform (GNC)-patients.

Figure 4: This radar diagram demonstrates EQ-5D items AD (Anxiety/Depression), MO (Mobility), PD (Pain/Discomfort), SC (Self-Care) and UA (Usual Activities) and graphically represents the distribution of the groups with respect to the dimensions in **(A)** PCI-first (PCF) vs. CABG-only (CO) and **(B)** guideline-conform (GCO)- vs. non-

conform (GNC)-patients. The radar diagrams were created using the “EQ-5D”-software (https://github.com/fragla/eq5d).

Table 1: Preoperative patient characteristics for PCI-first vs. CABG-only patients

Preoperative patient characteristics for PCI-first vs. CABG-only patients indicate no significant differences in baseline demographic data. Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CAD, cerebral arterial disease; CCS, Canadian Cardiovascular Society classification system; EuroScoreII, European System for Cardiac Operative Risk Evaluation II; LM, left main coronary artery; NYHA, New York Heart Association classification system; PAOD, peripheral arterial occlusive disease; LAD, proximal left anterior descending artery; STS, Society of Thoracic Surgeons - Scoring System for Mortality and Morbidity; SYNTAX, SYNergy between PCI with TAXus and Cardiac Surgery.

Table 2: Preoperative patient characteristics from guideline-conform (GCO) vs. non-conform (GNC) PCI treatment groups

This table reveals significantly higher SYNTAX-score as well as incidence for left main (LM) stenosis in GNC patients. Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CAD, cerebral arterial disease; CCS, Canadian Cardiovascular Society classification system; EuroScoreII, European System for Cardiac Operative Risk

Evaluation II; LM, left main coronary artery; NYHA, New York Heart Association classification system; PAOD, peripheral arterial occlusive disease; LAD, proximal left anterior descending artery; STS, Society of Thoracic Surgeons - Scoring System for Mortality and Morbidity; SYNTAX, SYNergy between PCI with TAXus and Cardiac Surgery.

Table 3: Postoperative outcome for PCI-first (PCF) vs. CABG-only (CO) patients

This table reveals no significant differences with respect to postoperative outcome between the two groups. Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CVVH, Continuous veno-venous hemofiltration; d, days; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; h, hours; IABP, intra-aortic balloon pump; ICU, intensive care unit; RBC**,** red blood cell; SAPS II, Simplified Acute Physiology Score II; TISS-10, Therapeutic Intervention Scoring System (TISS); U, unit.

Table 4: Postoperative outcome for guideline-conform (GCO) vs. non-conform (GNC) treatment

Comparable outcomes are observed with respect to death, adverse events, risk and nurse workload scores and length of hospital stay. Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CVVH, Continuous veno-venous hemofiltration; d, days; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; h, hours; IABP, intra-aortic balloon pump; ICU, intensive care unit; RBC, red blood cell; SAPS II, Simplified Acute Physiology Score II; TISS-10, Therapeutic Intervention Scoring System (TISS); U, unit.

Table 5: Follow-up data for PCI-first (PCF) vs. CABG-only (CO) patients

This table shows significant higher incidence of myocardial infarction (MI), angiography and Stent implantation in PCF. Interestingly, State of health is significantly better in CO-patients. Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). *p*<0.05 was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. ACB, aorto-coronary bypass surgery; MI, myocardial infarction.

Table 6: Follow-up data for guideline-conform (GCO) vs. non-conform (GNC) treatment

This table shows significant higher incidence of Stent implantation in GNC- compared to GCO-patients. In the latter, also, state of health is significantly better. Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). *p*<0.05 was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. ACB, aorto-coronary bypass surgery; MI, myocardial infarction.

Supplementary Table 2S: Preoperative patient characteristics from guideline-conform (GCO) vs. non-conform (GNC) PCI according to 2018 ECS/EACTS-guidelines

Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CAD, cerebral arterial disease; CCS, Canadian Cardiovascular Society classification system; EuroScoreII, European System for Cardiac Operative Risk Evaluation II; LM, left main coronary artery; NYHA, New York Heart Association classification system; PAOD, peripheral arterial occlusive disease; LAD, proximal left anterior descending artery; STS, Society of Thoracic Surgeons - Scoring System for Mortality and Morbidity; SYNTAX, SYNergy between PCI with TAXus and Cardiac Surgery.

Supplementary Table 3S: Postoperative outcome in PCI-first (PCF) patients with subgroups: 1-/2-vessel CAD vs. 3-vessel CAD

Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CVVH, Continuous veno-venous hemofiltration; d, days; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; h, hours; IABP, intra-aortic balloon pump; ICU, intensive care unit; RBC, red blood cell; SAPS II, Simplified Acute Physiology Score II; TISS-10, Therapeutic Intervention Scoring System (TISS); U, unit.

Supplementary Table 4S: Postoperative outcome for guideline-conform (GCO) vs. non-conform (GNC) treatment of patients according to 2018 ECS/EACTS-guidelines

Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. CVVH, Continuous veno-venous hemofiltration; d, days; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; h, hours; IABP, intra-aortic balloon pump; ICU, intensive care unit; RBC, red blood cell; SAPS II, Simplified Acute Physiology Score II; TISS-10, Therapeutic Intervention Scoring System (TISS); U, unit.

Supplementary Table 6S: Follow-up data for guideline-conform (GCO) vs. non-conform (GNC) treatment according to 2018 ECS/EACTS-guidelines

Values are expressed as mean ± standard deviation, or as number and percentage (in bracket). $p<0.05$ was considered statistically significant, and significant changes are displayed in italics. [1]t-test; [2]Mann-Whitney-U; [3]Chi-Square test. ACB, aorto-coronary bypass surgery; MI, myocardial infarction.

Supplementary Table 2S	**Guideline-conform treatment 2018 (GCO; n=58)**	**Guideline-nonconform treatment 2018 (GNC; n=33)**	***p*-Value**
Age (y)	64.86 ± 9.59	65.88 ± 9.56	0.931²
Gender			
Female	15/58 (25.9%)	5/33 (15.1%)	0.236³
Male	43/58 (74.1%)	28/33 (84.8%)	0.236³
Arterial Hypertension	42/58 (72.4%)	24/33 (72.7%)	0.974³
Diabetes mellitus	13/41 (31.7%)	16/28 (57.1%)	*0.036³*
PAOD	11/56 (19.6%)	5/33 (15.1%)	0.594³
CAD	8/56 (14.3%)	6/33 (18.2%)	0.626³
hyperlipidaemia	32/58 (55.2%)	18/33 (54.5%)	0.954³
smoker	16/58 (27.6%)	9/33 (27.3%)	0.974³
former stroke	4/58 (6.9%)	4/33 (12.1%)	0.397³
NYHA-classification			0.589³
I	6 (10.3%)	1 (3.0%)	
II	18 (31.0%)	12 (36.4%)	
III	27 (46.6%)	17 (51.5%)	
IV	7 (12.1%)	3 (9.1%)	
CCS-classification			0.775³
0	8 (13.8%)	5 (15.1%)	

I	8 (13.8%)	5 (15.1%)	
II	26 (44.8%)	11 (33.3%)	
III	10 (17.2%)	9 (27.3%)	
IV	6 (10.3%)	3 (9.1%)	
EuroScore II	4.66 ± 2.66 (/ 50 pts.)	4.84 ± 3.34 (/ 31 pts.)	0.871²
STS Mortality	1.93 ± 3.45 (/ 50 pts.)	2.62 ± 6.09 (/ 31 pts.)	0.992²
STS Morbidity	13.93 ± 13.31 (/ 50 pts.)	15.18 ± 14.21 (/ 31 pts.)	0.831²
SYNTAX-score before PCI (arithmetic mean)	18.68 ± 10.34 (/ 57 pts.)	24.38 ± 6.43 (/ 33 pts.)	*0.007¹*
SYNTAX-score before CABG	21.10 ± 7.45 (/ 50 pts.)	21.65 ± 8.39 (/ 30 pts.)	0.650¹
LM stenosis	10/57 (17.5%)	18/33 (54.5%)	*<0.001³*
Prox. LAD stenosis	35/57 (57.9%)	26/33 (78.8%)	0.089³

Supplementary Table 3S	**PCI-first (PCF; n=213)**		***p*-Value**
	1-/2-vessel CAD (n=20)	3-vessel CAD (n=178)	
Mobilization on the first postoperative day	9/19 (47.4%)	73/176 (41.5%)	0.621³
wound healing disorder	4/19 (21.0%)	22/175 (12.6%)	0.303³
Delirium	2/18 (11.1%)	15/164 (9.1%)	0.786³

CVVH	1/20 (5%)	8/174 (4.6%)	0.935[3]
IABP	0/19 (0%)	1/175 (0.6%)	0.741[3]
ECMO	0/19 (0%)	1/175 (0.6%)	0.741[3]
Duration of ventilation (h)	76.16 ± 354.77 (/ 19 pts.)	38.20 ± 85.64 (/ 173 pts.)	*0.031*[2]
ICU stay (d)	4.45 ± 9.01 (/ 20 pts)	3.59 ± 4.74 (/ 177 pts.)	0.565[2]
Length of hospital stay (d)	16.33 ± 7.91 (/ 18 pts)	18.16 ± 10.67 (/ 175 pts.)	0.353[2]
RBC (U)	1.21 ± 1.62 (/ 19 pts)	2.20 ± 3.27 (/ 175 pts.)	0.267[2]
Platelet transfusion (U)	0 (/ 19 pts)	0.35 ± 0.91 (/ 175 pts.)	*0.043*[2]
FFP (U)	0.26 ± 0.93 (/ 19 pts)	1.03 ± 2.41 (/ 175 pts.)	0.275[2]
SAPS-II 24h	28.30 ± 7.27 (/ 10 pts)	30.35 ± 10.75 (/ 118 pts.)	0.578[2]
TISS-10 24h	28.00 ± 9.53 (/ 10 pts)	23.57 ± 5.80 (/ 118 pts.)	0.197[2]
30-days Mortality	-	3/10 (30%)	-
Death	0/17 (0%)	10/125 (8.0%)	0.226[3]

Supplementary	**Guideline-conform**	**Guideline-nonconform**	***p*-Value**

Table 4S	treatment 2018 (GCO; n=58)	treatment 2018 (GNC; n=33)	
Mobilization on the first postoperative day	17/50 (34%)	13/31 (41.9%)	0.472[3]
wound healing disorder	7/50 (14%)	3/31 (9.7%)	0.565[3]
Delirium	4/47 (8.5%)	1/27 (3.7%)	0.428[3]
CVVH	5/58 (8.6%)	2/31 (6.4%)	0.717[3]
IABP	0/40 (0%)	1/31 (3.2%)	0.206[3]
ECMO	1/49 (2%)	0/31 (0%)	0.423[3]
Duration of ventilation (h)	52.61 ± 122.51 (/ 49 pts.)	25.40 ± 25.14 (/ 30 pts.)	0.206[2]
ICU time (d)	4.14 ± 4.53 (/ 58 pts.)	3.45 ± 3.34 (/ 33 pts.)	0.707[2]
Length of hospital stay (d)	18.18 ± 11.02 (/ 49 pts.)	16.71 ±7.15 (/ 31 pts.)	0.941[2]
RBC (U)	3.08 ± 4.42 (/ 50 pts.)	1.58 ± 2.33 (/ 31 pts.)	0.101[2]
Platelet transfusion (U)	0.54 ± 1.34 (/ 50 pts.)	0.29 ± 0.64 (/ 31 pts.)	0.733[2]
FFP (U)	1.44 ± 3.26 (/ 50 pts.)	0.90 ± 1.92 (/ 31 pts.)	0.516[2]
SAPS-II 24h	31.48 ± 11.76 (/ 40 pts.)	34.15 ± 12.95 (/ 20 pts.)	0.174[2]
TISS-10 24h	24.85 ± 6.79 (/ 40 pts.)	23.20 ± 4.11 (/ 20 pts.)	0.503[2]
30-days Mortality	2/4 (50%)	1/1 (100%)	0.361[3]
Total death	4/44 (9.1%)	1/23 (4.3%)	0.483[3]

Supplementary Table 6S	**Guideline-conform treatment 2018 (GCO; n=58)**	**Guideline-nonconform treatment 2018 (GNC; n=33)**	***p*-Value**
State of health (0-100)	72.35 ± 18.17 (/ 34 pts.)	68.53 ± 15.49 (/ 17 of pts.)	0.273[2]
Degree of Care None 1 2 3 4 5	 33/36 (91.7%) 0/36 (0.0%) 2/36 (5.5%) 1/36 (2.8%) 0/36 (0.0%) 0/36 (0.0%)	 19/20 (95%) 1/20 (5%) 0/20 (0.0%) 0/20 (0.0%) 0/20 (0.0%) 0/20 (0.0%)	0.323[3]
Re-angiography	3/37 (8.1%)	7/23 (30.4%)	*0.024*[3]
Stent implantation	1/36 (2.8%)	3/21 (14.3%)	0.101[3]
Stroke	1/35 (2.9%)	1/20 (5%)	0.683[3]
MI	1/36 (2.8%)	2/21 (9.5%)	0.271[3]
Pace maker	0/35 (0.0%)	0/20 (0.0%)	-
ACB	0/36 (0.0%)	0/20 (0.0%)	-

Table 1: Preoperative patient characteristics for PCI-first vs. CABG-only patients

	PCI-first (PCF; n=213)	**CABG-only (CO; n=784)**	***p*-Value**
Age (y)	66.92 ± 9.23	67.91 ± 9.21	0.124²
Gender			
Female	40/213 (18.8%)	146/783 (18.6%)	0.965³
Male	173/213 (81.2%)	637/783 (81.4%)	0.965³
Arterial Hypertension	162/213 (76.1%)	598/783 (76.4%)	0.923³
Diabetes mellitus	72/160 (45.0%)	235/594 (39.6%)	0.459³
PAOD	41/211 (19.4%)	126/783 (16.1%)	0.250³
CAD	38/211 (18.0%)	137/783 (17.5%)	0.862³
hyperlipidaemia	136/213 (63.8%)	482/783 (61.6%)	0.541³
smoker	62/213 (29.1%)	231/783 (29.5%)	0.911³
former stroke	26/213 (12.2%)	96/783 (12.3%)	0.983³
NYHA-classification			0.674³
I	15/213 (7.0%)	47/782 (6.0%)	
II	71/213 (33.3%)	232/782 (29.7%)	
III	103/213 (48.4%)	406/782 (51.9%)	
IV	24/213 (11.3%)	94/782 (12.0%)	
CCS-classification			0.774³

0	33/213 (15.5%)	97/782 (12.4%)	
I	28/213 (13.1%)	100/782 (12.8%)	
II	80/213 (37.6%)	316/782 (40.4%)	
III	47/213 (22.1%)	183/782 (23.4%)	
IV	25/213(11.7%)	86/782 (11.0%)	
EuroScore II	4.57 ± 2.89 (/ 198 pts.)	4.89 ± 3.41 (/ 748 pts.)	0.309²
STS Mortality	1.82 ± 3.18 (/ 198 pts.)	1.94 ± 3.11 (/ 746 pts.)	0.180²
STS Morbidity	13.74 ± 10.41 (/ 198 pts.)	14.40 ± 10.48 (/ 745 pts.)	0.254²
SYNTAX-score before CABG	22.71 ± 8.01 (/ 197 pts.)	25.59 ± 7.98 (/ 743 pts.)	0.843¹

Table 2: Preoperative patient characteristics from guideline-conform (GCO) vs. non-conform (GNC) PCI treatment groups

	Guideline-conform treatment (GCO; n=67)	**Guideline-nonconform treatment (GNC; n=24)**	***p*-Value**
Age (y)	64.61 ± 9.34	66.96 ± 10.08	0.449²
Gender			
Female	16/67 (23.9%)	4/24 (16.7%)	0.464³
Male	51/67 (76.1%)	20/24 (83.3%)	0.464³
Arterial Hypertension	51/67 (76.1%)	15/24 (62.5%)	0.200³
Diabetes mellitus	21/50 (42.0%)	8/19 (42.1%)	0.821³
PAOD	14/65 (21.5%)	2/24 (8.3%)	0.150³
CAD	9/65 (13.8%)	5/24 (20.8%)	0.422³
hyperlipidaemia	40/67 (59.7%)	10/24 (41.7%)	0.128³
smoker	17/67 (25.4%)	8/24 (33.3%)	0.453³
former stroke	5/67 (7.5%)	3/24(12.5%)	0.455³
NYHA-classification			0.812³
I	6 (9.0%)	1 (4.2%)	
II	21 (31.3%)	9 (37.5%)	
III	32 (47.8%)	12 (50.0%)	

IV	8 (11.9%)	2 (8.3%)	
CCS-classification			0.498³
0	11 (16.4%)	2 (8.3%)	
I	8 (11.9%)	5 (20.8%)	“
II	29 (43.3%)	8 (33.3%)	“
III	12 (17.9%)	7 (29.2%)	“
IV	7 (10.4%)	2 (8.3%)	“
EuroScore II	4.63 ± 2.72 (/ 59 pts.)	5.00 ± 3.45 (/ 22 pts.)	0.897²
STS Mortality	1.82 ± 3.20 (/ 59 pts.)	3.20 ± 7.17 (/ 22 pts.)	0.924²
STS Morbidity	13.70 ± 12.50 (/ 59 pts.)	16.31 ± 16.33 (/ 22 pts.)	0.824²
SYNTAX-score before PCI (arithmetic mean)	18.63 ± 9.81 (/ 66 pts.)	26.67 ± 5.07	*0.005¹*
SYNTAX-score before CABG	21.26 ± 7.21 (/ 58 pts.)	21.43 ± 9.26 (/ 22 pts.)	0.201¹
LM stenosis	13/66 (19.7%)	9/24 (37.5%)	*<0.001³*
Prox. LAD stenosis	41/66 (62.1%)	20/24 (83.3%)	0.057³

Table 3: Postoperative outcome for PCI-first (PCF) vs. CABG-only (CO) patients

	PCI-first (PCF; n=213)	**CABG-only (CO; n=784)**	***p*-Value**
Mobilization on the first postoperative day	82/196 (41.8%)	272/741 (36.7%)	0.082³
wound healing disorder	23/194 (11.7%)	80/733 (10.7%)	0.884³
Delirium	17/185 (9.2%)	88/680 (12.9%)	0.166³
CVVH	10/209 (4.8%)	41/781 (5.2%)	0.787³
IABP	1/197 (0.5%)	21/746 (2.8%)	0.056³
ECMO	1/197 (0.5%)	13/747 (1.7%)	0.203³
Duration of ventilation (h)	41.68 ± 112.51 (/ 195 pts.)	53.20 ± 155.87 (/ 730 pts.)	0.959²
ICU stay (d)	3.78 ± 5.46 (/ 212 pts)	4.40 ± 8.09 (/ 779 pts.)	0.392²
Length of hospital stay (d)	17.98 ± 10.37 (/ 196 pts)	18.09 ± 13.10 (of 743 pts.)	0.265²
RBC (U)	2.10 ± 3.14 (/ 197 pts)	1.98 ± 4.40 (/ 740 pts.)	0.086²
Platelet transfusion (U)	0.31 ± 0.86 (/ 197 pts)	0.33 ± 1.36 (/ 741 pts.)	0.320²
FFP (U)	0.94 ± 2.30 (/ 197 pts)	1.03 ± 3.23 (/ 740 pts.)	0.798²
SAPS-II 24h	30.38 ± 10.32 (/ 138 pts)	30.28 ± 9.40 (/ 515 pts.)	0.911²

TISS-10 24h	24.01 ± 6.14 (/ 138 pts)	23.63 ± 6.99 (/ 516 pts.)	0.755²
30-days Mortality	3/154 (1.95%)	27/594 (4.55%)	0.312³
Death	11/154 (7.1%)	62/594 (10.4%)	0.220³

Table 4: Postoperative outcome for guideline-conform (GCO) vs. non-conform (GNC) treatment

	Guideline-conform treatment (GCO; n=67)	**Guideline-nonconform treatment (GNC; n=24)**	***p*-Value**
Mobilization on the first postoperative day	21/59 (35.6%)	9/22 (40.9%)	0.659³
wound healing disorder	8/59 (13.6%)	2/20 (9.1%)	0.771³
Delirium	5/53 (9.4%)	0/21 (0.0%)	0.145³
CVVH	6/66 (9.1%)	1/23 (4.3%)	0.467³
IABP	0/58 (0.0%)	1/22 (4.5%)	0.102³
ECMO	1/58 (1.7%)	0/22 (0.0%)	0.535³
Duration of ventilation (h)	50.56 ± 114.76 (/ 57 pts.)	20.82 ± 7.06 (/ 22 pts.)	0.100²
ICU time (d)	4.12 ± 4.33	3.25 ± 3.54	0.386²
Length of hospital stay (d)	17.93 ± 10.35 (/ 58 pts.)	16.77 ±7.78 (/ 22 pts.)	0.974²
RBC (U)	2.97 ± 4.25 (/ 59 pts.)	1.27 ± 1.86 (/ 22 pts.)	0.080²
Platelet transfusion (U)	0.49 ± 1.27 (/ 59 pts.)	0.32 ± 0.65 (/ 22 pts.)	0.899²

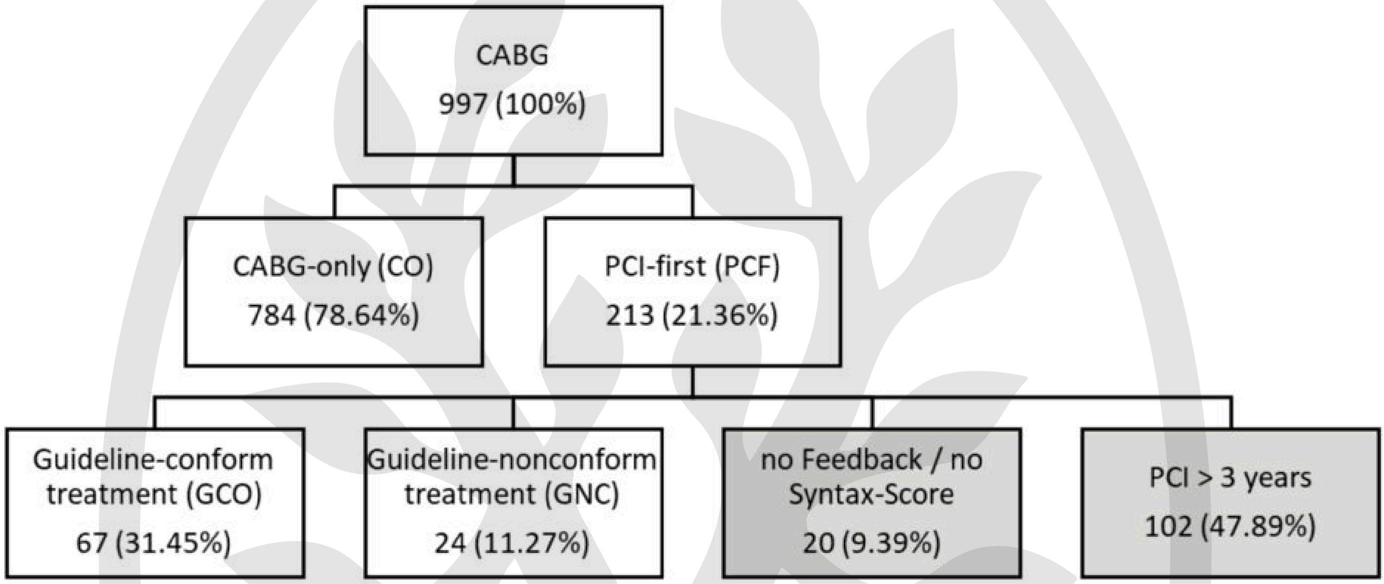
FFP (U)	1.29 ± 3.06 (/ 59 pts.)	1.09 ± 2.11 (/ 22 pts.)	0.971[2]
SAPS-II 24h	31.82 ± 11.35 (/ 44 pts.)	33.88 ± 14.35 (/ 16 pts.)	0.487[2]
TISS-10 24h	24.57 ± 6.69 (/ 44 pts.)	23.56 ± 3.83 (/ 16 pts.)	0.698[2]
30-days Mortality	2/49 (4.1%)	1/18 (5.6%)	0.361[3]
Total death	4/49 (8.2%)	1/18 (5.6%)	0.719[3]

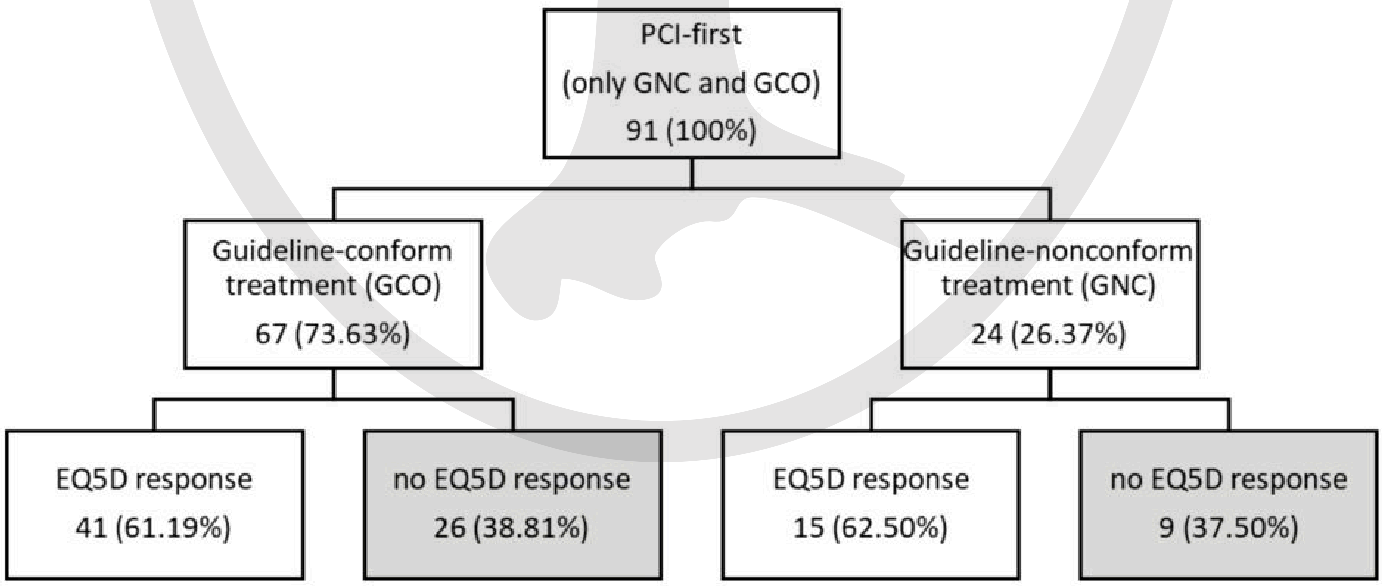
Table 5: Follow-up data for PCI-first (PCF) vs. CABG-only (CO) patients

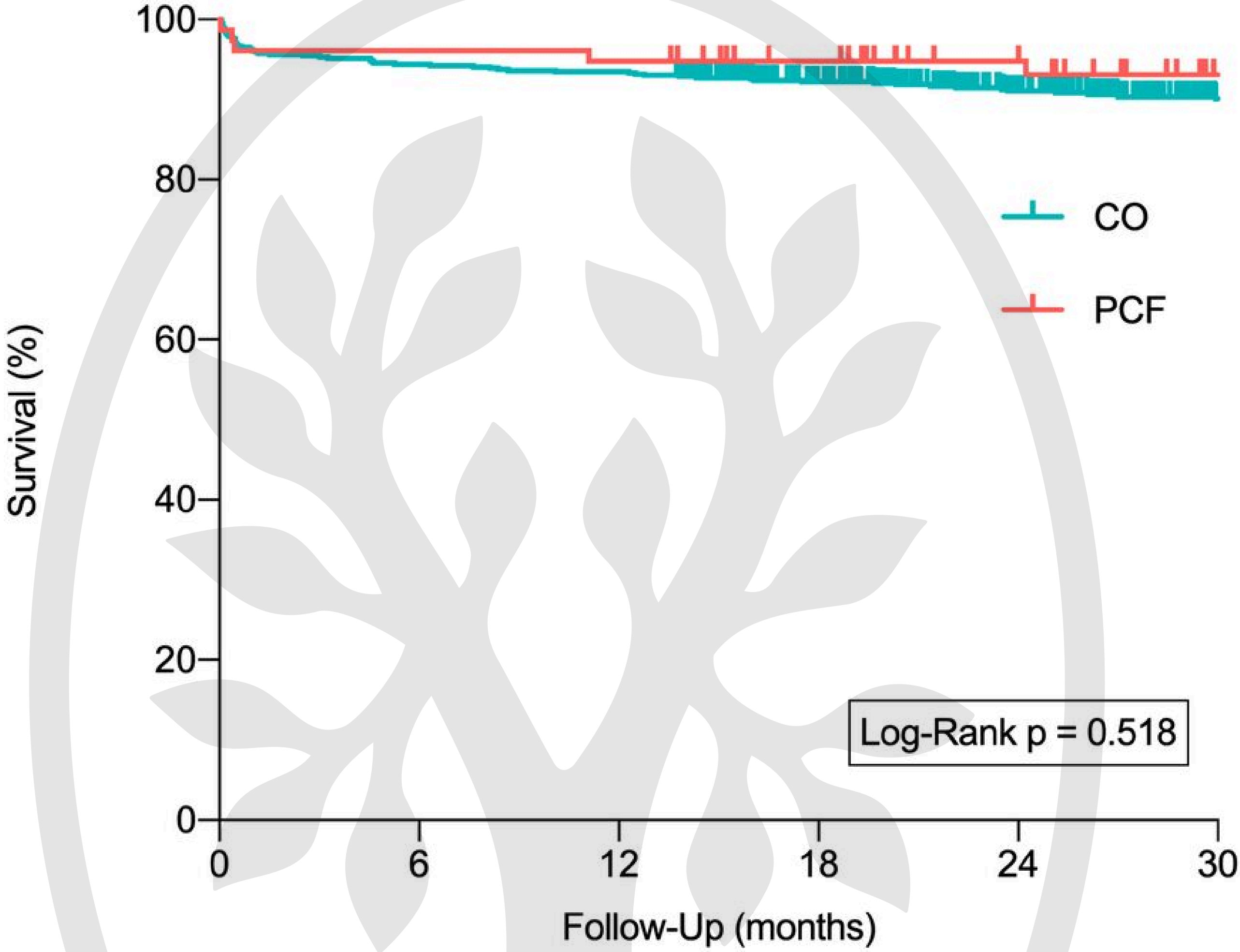
	PCI-first (PCF; n=213)	**CABG-only (CO; n=784)**	***p*-Value**
State of health (0-100)	68.20 ± 17.86 (/ 116 pts.)	72.48 ± 19.31 (/ 446 pts.)	*0.010*[2]
Degree of Care None 1 2 3 4 5	 119/132 (90.2%) 2/132 (1.5%) 7/132 (5.3%) 2/132 (1.5%) 0/132 (0.0%) 2/132 (1.5%)	 452/491 (92.1%) 12/491 (2.4%) 14/491 (2.9%) 8/491 (1.6%) 3/491 (0.6%) 2/491 (0.4%)	0.404[3]
Re-angiography	24/136 (17.6%)	45/501 (9.0%)	*0.004*[3]
Stent implantation	14/134 (10.4%)	15/498 (3.0%)	*<0.001*[3]
Stroke	5/133 (3.8%)	13/502 (2.6%)	0.470[3]
MI	5/133 (3.8%)	5/499 (1.0%)	*0.024*[3]
Pace maker	1/131 (0.8%)	11/501 (2.2%)	0.285[3]
ACB	0/132 (0.0%)	1/499 (0.2%)	0.607[3]

Table 6: Follow-up data for guideline-conform (GCO) vs. non-conform (GNC) treatment

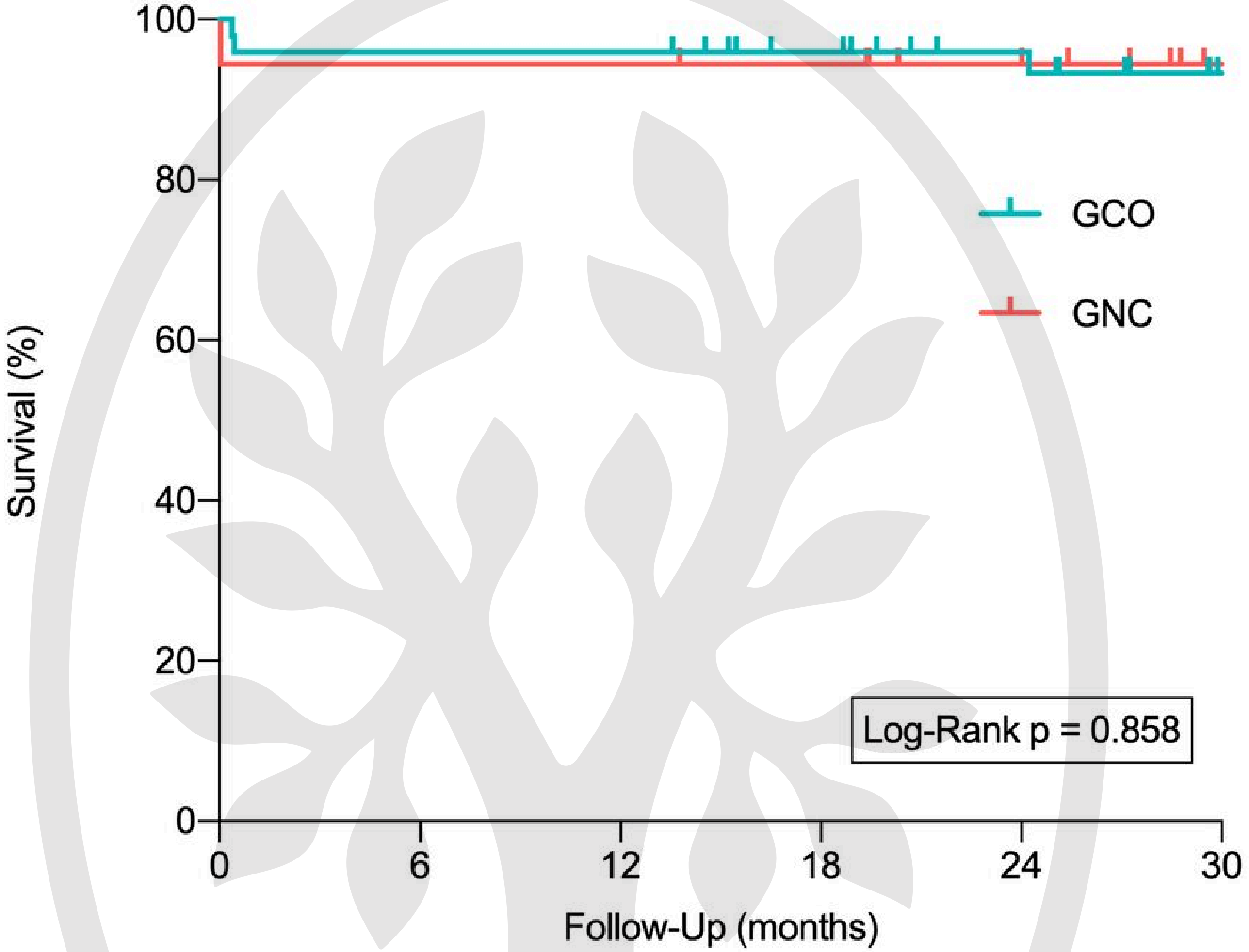
	Guideline-conform treatment (GCO; n=67)	**Guideline-nonconform tr. (GNC; n=24)**	***p*-Value**
State of health (0-100)	73.42 ± 17.66 (/ 38 pts.)	64.23 ± 14.56 (/ 13 of pts.)	*0.041*²
Degree of Care			0.280³
None	38/41 (92.7%)	14/15 (93.3%)	
1	0/41 (0.0%)	1/15 (6.7%)	
2	2/41 (4.9%)	0/15 (0.0%)	
3	1/41 (2.4%)	0/15 (0.0%)	
4	0/41 (0.0%)	0/15 (0.0%)	
5	0/41 (0.0%)	0/15 (0.0%)	
Re-angiography	5/43 (11.6%)	5/17 (29.4%)	0.096³
Stent implantation	1/41 (2.4%)	3/16 (18.8%)	*0.030*³
Stroke	1/40 (2.5%)	1/15 (6.7%)	0.462³
MI	1/41 (2.4%)	2/16 (12.5%)	0.126³
Pace maker	0/41 (0.0%)	0/15 (0.0%)	-
ACB	0/41 (0.0%)	0/15 (0.0%)	-


CABG
997 (100%)
CABG-only (CO)
784 (78.64%)
PCI-first (PCF)
213 (21.36%)
Guideline-conform treatment (GCO)
67 (31.45%)
Guideline-nonconform treatment (GNC)
24 (11.27%)
no Feedback / no Syntax-Score
20 (9.39%)
PCI > 3 years
102 (47.89%)

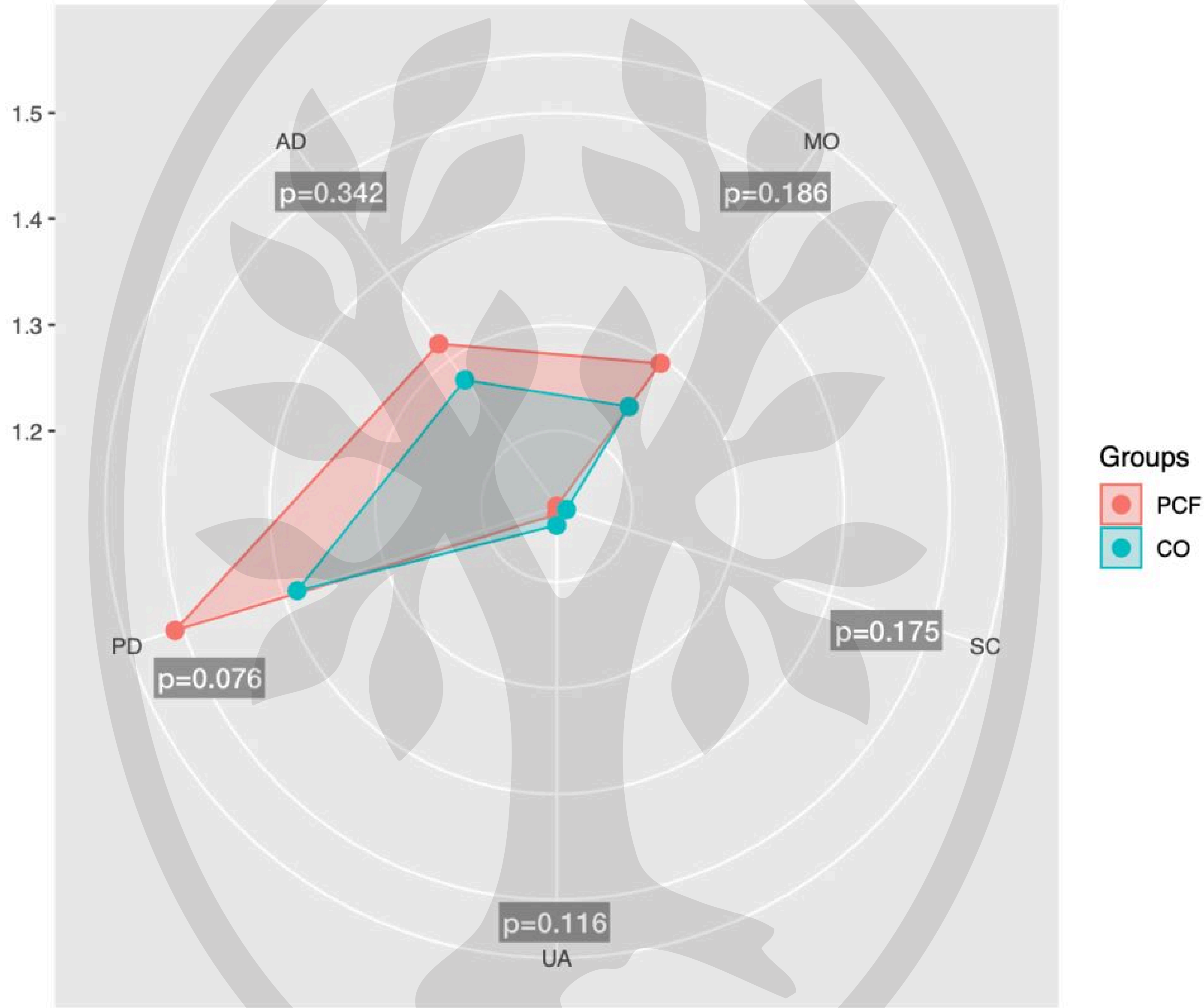

PCI-first
(only GNC and GCO)
91 (100%)
Guideline-conform treatment (GCO)
67 (73.63%)
Guideline-nonconform treatment (GNC)
24 (26.37%)
EQ5D response
41 (61.19%)
no EQ5D response
26 (38.81%)
EQ5D response
15 (62.50%)
no EQ5D response
9 (37.50%)

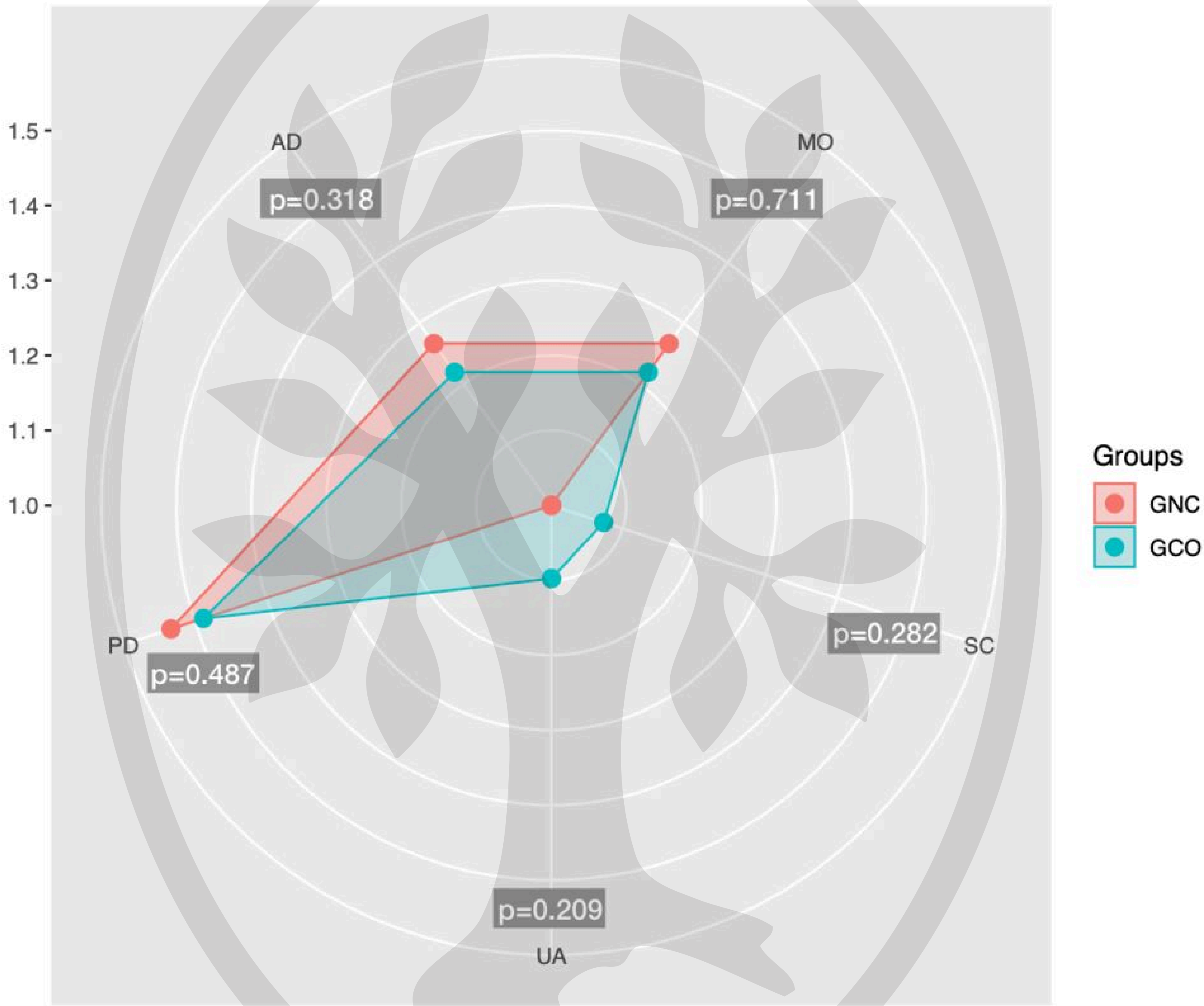


	0	6	12	18	24	30
Survival (%)	100	94	93	93	91	90
Patients at Risk	660	624	618	533	429	332
Survival (%)	100	96	95	95	95	93
Patients at Risk	77	75	74	67	56	41



Survival (%)	100	96	96	96	96	93
Patients at Risk	49	48	48	43	38	30
Survival (%)	100	96	96	96	96	93
Patients at Risk	18	17	17	17	12	6


1.5
1.4
1.3
1.2
AD
MO
p=0.342
p=0.186
PD
p=0.076
p=0.175
SC
p=0.116
UA
Groups
PCF
CO



1.5
1.4
1.3
1.2
1.1
1.0
AD
MO
p=0.318
p=0.711
PD
p=0.487
p=0.282
SC
p=0.209
UA
Groups
GNC
GCO

3. Danksagung

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