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ORIGINAL ARTICLE

Clinical practice patterns in revascularization of diabetic patients with coronary heart disease: nationwide register study

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ABSTRACT

Aims: To compare diabetic patients with coronary heart disease (CHD) needing revascularization to corresponding non-diabetic patients in terms of revascularization methods, comorbidities and urgency of procedure. We also examined the impact of patient characteristics and comorbidities on the revascularization method.

Methods: We identified all diabetic ($n = 33{,}018$) and non-diabetic ($n = 106{,}224$) patients with first-ever, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) from electronic health records in Finland between 2000 and 2015.

Results: Overall, PCI was the most common revascularization method. PCI outnumbered CABG in women and men both in diabetic and non-diabetic patients. However, diabetic patients were more likely to undergo CABG than PCI (OR 1.30; 95% CI 1.27–1.34, adjusted for age, gender, region of residence and procedure year). Moreover, 26.9% of diabetic patients' urgent procedures were CABG compared to 21.6% in non-diabetic patients ($p<.001$). Among diabetic patients, prior myocardial infarction was associated with increased odds of CABG, whereas female gender, atrial fibrillation, congestive heart failure, hypertension and later procedure year were associated with lower odds of CABG.

Conclusions: CABG has been performed more frequently in diabetic than in non-diabetic CHD patients. Nevertheless, PCI was the dominant revascularization method over CABG both in diabetic and non-diabetic patients.

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KEY MESSAGES

- PCI was the dominant revascularization method in both diabetic and non-diabetic patients. Diabetic patients were more likely to undergo CABG than PCI when compared to non-diabetic patients (OR: 1.30; CI 1.27–1.34).
- Diabetic patients underwent urgent CABG procedures more often than non-diabetic patients and had more comorbidities compared to non-diabetic patients.

Abbreviations: AF: atrial fibrillation; BMS: bare metal stent; CABG: coronary artery bypass grafting; CHD: coronary heart disease; CHF: chronic heart failure; DES: drug-eluting stent; ICD: International Classification of Diseases; MI: myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; RCT: randomised controlled trial; STEMI: ST-segment elevation myocardial infarction; SYNTAX score: Synergy between PCI with Taxus and Cardiac Surgery score

Introduction

The optimal method of myocardial revascularization in diabetic patients has been debated for decades. Numerous randomised trials have been conducted on this topic, with the conclusion that the operative treatment of choice for diabetic patients' coronary heart disease should be CABG rather than PCI [1–4]. After the advent of drug-eluting stents (DES) and the development of second-generation DES's, the difference in mortality between PCI and CABG has narrowed [5–7]. Although the treatment guidelines are still in favour of CABG in diabetic patients with complex CHD, PCI has become an alternative for diabetic patients with less complex CHD [2]. Potential advantages of PCI with stenting also include lower risk of stroke complications when compared to CABG [8–10].

In the face of this situation, and despite the fact that most guidelines tend to favour CABG, data describing actual clinical practice patterns of diabetic patients' revascularizations are scarce. Specifically, there is an unmet need for data describing patient selection, gender distribution and the relative

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proportion of CABG versus PCI in diabetic patients. Choosing the most suitable revascularization method for diabetic patients has huge economic and public health implications, as diabetes constitutes 8.3–19.4% of total healthcare costs, and the projected number of diabetic patients is expected to increase by approximately 50% within the next 25 years [11].

Our aim was to assess the relative proportions of incident PCI and CABG procedures among diabetic and non-diabetic patients in Finland in 2000–2015. We also examined the impact of patient characteristics and comorbidities on the method of revascularization. Finally, we examined whether either revascularization method was applied more frequently for patients requiring urgent revascularization.

Methods

All patients who underwent coronary revascularization in Finland during 2000–2015 were identified using the nationwide Hospital Discharge Register. This register has been assembled from electronic templates filled out by the treating physicians for every invasive cardiac procedure. The register contains information on diagnoses assigned and procedures performed during the patient care periods. Further details about this register have recently been described [12]. Information on the procedures has been registered since 1996 under codes defined by the Nordic Medico-Statistical Committee. The diagnoses are recorded according to the Finnish version of the ICD-10 codes. Personal ID code, unique to each permanent resident of Finland, was used for distinguishing first and repeated procedures of the same individual, as well as for linking the Hospital Discharge Register with the other Finnish electronic health care registers.

Diabetic patients were identified by ICD-10 codes E10 or E11, or additionally, if an entitlement to reimbursements for antihyperglycemic medications had been recorded in the Drug Reimbursement Register. To describe patient comorbidities, we included diagnoses for hypertension (ICD-10 code I10), chronic heart failure (ICD-10 codes I11, I50), atrial fibrillation (ICD-10 code I48), previous stroke (ICD-10 codes I61, I63 (excluding code I63.6), I64 and I60.0–I60.9 (subarachnoid haemorrhage)) and previous myocardial infarction (MI; ICD-10 codes I21, I22). Chronic heart failure was also considered, if the patient was entitled to special reimbursement for the costs of heart failure medications. We analysed the comorbidities based first on the diabetes status and then on the revascularization method (PCI or CABG). A procedure was defined urgent if it was necessary to perform it as an emergency procedure or within 7 days after hospitalisation. A procedure carried out later than that was considered elective. If a CABG followed PCI within the same 7-day period, then CABG was considered as incident overriding the PCI procedure.

Statistical methods

We pooled data on incident revascularization procedures from 2000 to 2015, and to better distinguish potential alterations in practice patterns, we also performed separate analysis for the most recent years 2012–2015. We examined the distributions of CABG versus PCI procedures in diabetic and non-diabetic individuals in 6 subgroups: "diabetic", "non-diabetic", "male diabetic", "female diabetic", "male non-diabetic" and "female non-diabetic" patients. Trends in patient characteristics across the time strata were compared using the Cochran-Armitage trend test for categorical variables and regression analysis for continuous variables. Logistic regression, adjusting for age, gender, area of residence, and year of procedure, was used for examining the probability of diabetic patients to have CABG vs. PCI. Likewise, logistic regression was used for analysing whether the patient characteristics had an impact on the choice of revascularization method. We considered $p<.05$ to be statistically significant in all analyses. 95% confidence intervals (CI) are presented when appropriate. All analyses were carried out using R statistical software version 3.6.0 (R Core Team, 2019).

Results

Patient characteristics

A total of 139,242 patients underwent revascularizations in Finland during 2000–2015. Of all revascularized patients, 24% ($n = 33{,}018$) had diabetes, whereas 76% ($n = 106{,}224$) did not. The proportion of women was higher among diabetic patients than among non-diabetic patients (32.2%, $n = 10{,}623$ vs. 27.5%, $n = 29{,}212$, $p<.001$). During the study period of 2000–2015, the overall mean age of CABG patients was 67.3 years and of PCI patients 66.5 years. During the study period, the mean age of patients undergoing either PCI or CABG increased from 65 in 2000–2003 to 69 in 2012–2015, and the frequency of comorbidities, except previous MI, increased (Table 1). The proportion of diabetic patients increased among both PCI and CABG groups during the study period from 2000 to 2015. Women accounted for 25% of CABG and 31% of PCI revascularizations. The

Table 1. Patient characteristics.

Characteristics	Overall	2000–2003	2004–2007	2008–2011	2012–2015	p-Value
Total						
N	139,242	32,337	37,867	33,518	35,520	
Age	66.8 (10.8)	64.9 (10.3)	66.3 (10.5)	67.3 (10.8)	68.6 (11.2)	<.001
Women	39,805 (28.6)	9041 (28.0)	10,873 (28.7)	9364 (27.9)	10,527 (29.6)	<.001
Urgent	57,758 (54.0)	NA	17,435 (46.0)	19,217 (57.3)	21,106 (59.4)	<.001
Previous MI	32,317 (23.2)	11,580 (35.8)	8309 (21.9)	6264 (18.7)	6164 (17.4)	<.001
Previous stroke	8540 (6.1)	1702 (5.3)	2175 (5.7)	1956 (5.8)	2707 (7.6)	<.001
Previous AF	13,128 (9.4)	2152 (6.7)	3222 (8.5)	3283 (9.8)	4471 (12.6)	<.001
CHF	81,446 (58.5)	17,770 (55.0)	21,082 (55.7)	20,350 (60.7)	22,244 (62.6)	<.001
Hypertension	49,717 (35.7)	9004 (27.8)	13,211 (34.9)	12,917 (38.5)	14,585 (41.1)	<.001
Diabetic	33,018 (23.7)	6445 (19.9)	8353 (22.1)	8413 (25.1)	9807 (27.6)	<.001
CABG						
N	49,749	16,851	13,980	10,606	8312	
Age	67.3 (9.5)	66.0 (9.5)	67.2 (9.3)	68.1 (9.3)	69.0 (9.5)	<.001
Women	12,313 (24.8)	4401 (26.1)	3432 (24.5)	2483 (23.4)	1997 (24.0)	<.001
Urgent	13,164 (40.0)	NA	5513 (39.4)	4465 (42.1)	3186 (38.3)	.410
Previous MI	15,714 (31.6)	6607 (39.2)	3737 (26.7)	2901 (27.4)	2469 (29.7)	<.001
Previous stroke	3347 (6.7)	971 (5.8)	877 (6.3)	700 (6.6)	799 (9.6)	<.001
Previous AF	4435 (8.9)	1153 (6.8)	1175 (8.4)	1062 (10.0)	1045 (12.6)	<.001
CHF	23,778 (47.8)	8177 (48.5)	6339 (45.3)	5108 (48.2)	4154 (50.0)	.021
Hypertension	17323 (34.8)	4732 (28.1)	4994 (35.7)	4142 (39.1)	3455 (41.6)	<.001
Diabetic	12,900 (25.9)	3742 (22.2)	3366 (24.1)	3108 (29.3)	2684 (32.3)	<.001
PCI						
N	89,493	15,486	23,887	22,912	27,208	
Age	66.5 (11.5)	63.6 (11.0)	65.8 (11.1)	66.9 (11.4)	68.5 (11.7)	<.001
Women	27,492 (30.7)	4640 (30.0)	7441 (31.2)	6881 (30.0)	8530 (31.4)	.042
Urgent	44,594 (60.3)	NA	11,922 (49.9)	14,752 (64.4)	17,920 (65.9)	<.001
Previous MI	16,603 (18.6)	4973 (32.1)	4572 (19.1)	3363 (14.7)	3695 (13.6)	<.001
Previous stroke	5193 (5.8)	1702 (4.7)	1298 (5.4)	1256 (5.5)	1908 (7.0)	<.001
Previous AF	8693 (9.7)	999 (6.5)	2047 (8.6)	2221 (9.7)	3426 (12.6)	<.001
CHF	57,668 (64.4)	9593 (61.9)	14,743 (61.7)	15,242 (66.5)	18,090 (66.5)	<.001
Hypertension	32,394 (36.2)	4272 (27.6)	8217 (34.4)	8775 (38.3)	11,130 (40.9)	<.001
Diabetic	20,118 (22.5)	2703 (17.5)	4987 (20.9)	5305 (23.2)	7123 (26.2)	<.001

Numbers are mean (±sd) for age, *n* (%) for other variables. NA: not applicable; MI: myocardial infarction; CHF: chronic heart failure; AF: atrial fibrillation; CABG: coronary artery bypass surgery; PCI: percutaneous coronary intervention. Procedure was considered urgent if it was performed within 7 days after hospitalisation. *p*-Values are for the test of linear trend across the time strata.

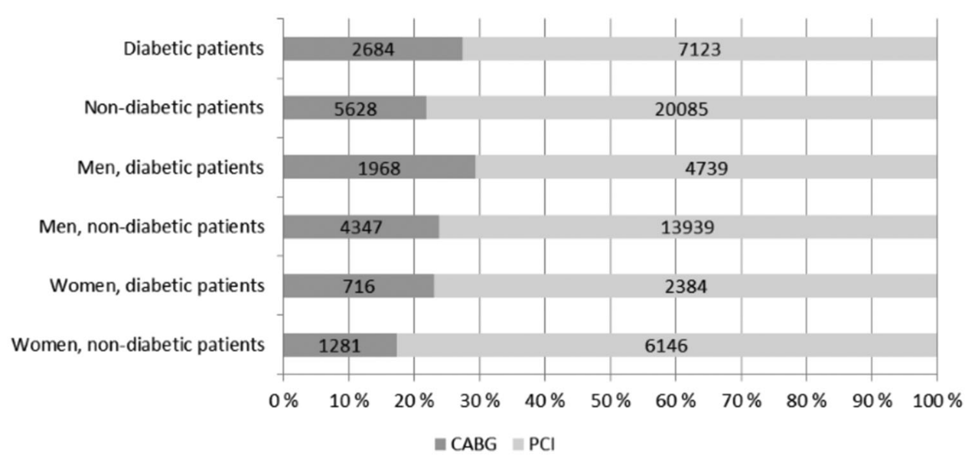

Figure 1 . Absolute numbers of revascularizations (PCI and CABG) in diabetic and non-diabetic patients in 2012–2015. The percentages are shown on the horizontal axis and the absolute numbers inside the columns. CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention.

proportion of urgent treatment increased from 46% in 2004–2007 to over 59% from 2012 onwards (Table 1).

Distribution of revascularizations

During the study period, the absolute number of CABG procedures decreased, whereas the absolute number of PCI procedures increased (Table 1). When the most recent years of our study period were examined separately, with patients divided by diabetes status and gender, we observed that PCIs outnumbered CABGs in every subgroup (Figure 1). However, after adjusting for age, gender, region of residence and year of procedure, patients with diabetes were more likely to undergo

CABG than PCI when compared to non-diabetic patients (OR: 1.30; CI 1.27–1.34) during the overall study period from 2000 to 2015. The findings were similar for both men (OR: 1.32; CI 1.28–1.36) and women (OR: 1.31; CI 1.25–1.37). Similar results were also observed in the most recent years 2012–2015 (Table 2).

Comorbidity

Diabetic patients undergoing any revascularization had more comorbidities (hypertension, CHF, previous stroke, and previous MI) than non-diabetic patients (Figure 2). Diabetic patients with hypertension or CHF underwent PCI more often than CABG, whereas those with previous MI had CABG done more often than PCI (Figure 3).

Characteristics having an impact on the method of revascularization

Among diabetic patients, previous MI was the only comorbidity increasing the odds for CABG as the revascularization method (Table 3). On the other hand, women with diabetes were less likely to undergo CABG than PCI. Atrial fibrillation, CHF, hypertension and later procedure year were associated with decreased odds of CABG over PCI (Table 3). For diabetic patients with previous stroke, both interventions were performed equally often (CABG 9% and PCI 9% p = NS; Figure 3). Age was not associated with the revascularization method.

Table 2. Odds ratios (OR) for CABG versus PCI in revascularized diabetic versus non-diabetic patients in 2012–2015.

	OR	Adjusted OR	Adjusted 2 OR
All	1.21 (1.18–1.24)	1.30 (1.27–1.34)	1.30 (1.26–1.33)
Men	1.23 (1.19–1.26)	1.32 (1.28–1.36)	1.32 (1.28–1.36)
Women	1.23 (1.17–1.28)	1.31 (1.25–1.37)	1.31 (1.25–1.38)

Numbers are odds ratios (OR), and 95% confidence intervals are shown in parentheses. Adjusted OR model includes age, year of procedure and region of residence as covariates. Adjusted 2 OR model includes valvular defect in addition to the covariates listed above. PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.

Urgency of revascularization procedures

Altogether, 54% ($n = 59{,}224$) of the revascularizations were performed as urgent procedures. The majority of the urgent revascularizations were PCIs (77%, $n = 44{,}594$), and a smaller proportion were CABGs (23%, $n = 13{,}164$) (Table1). When the proportions of the two revascularization methods among patients undergoing urgent procedures were compared, different distributions were observed in diabetic patients than in non-diabetic patients. In diabetic patients, 26.9% ($n = 3573$) of all urgent procedures were CABGs and 73.1% ($n = 9727$) were PCIs, whereas in non-diabetic patients, CABGs constituted 21.6% ($n = 9591$) and PCIs 78.4% ($n = 34{,}867$) of the urgent procedures ($p < .001$). Similar, but less pronounced differences were observed in elective procedures: among diabetic patients, 42.1% ($n = 5585$) of the elective procedures were CABGs and 57.9% ($n = 7688$) were PCIs, as

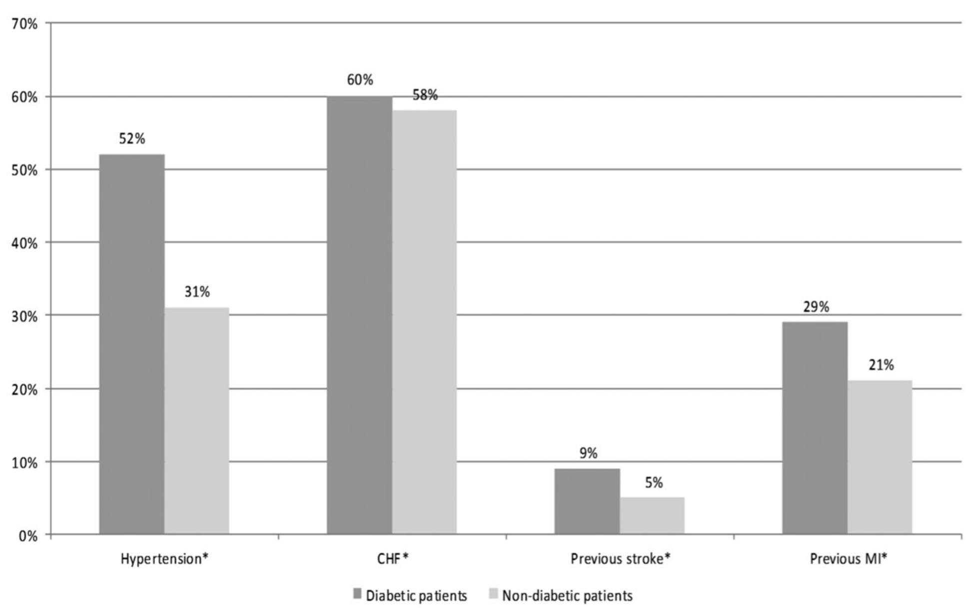

Figure 2. Comorbidity frequencies in diabetic patients and non-diabetic patients undergoing revascularization in Finland in 2000–2015. Adjusted model includes age, gender and region of residence as covariates. *$p < .001$. CHF: chronic heart failure; MI: myocardial infarction.

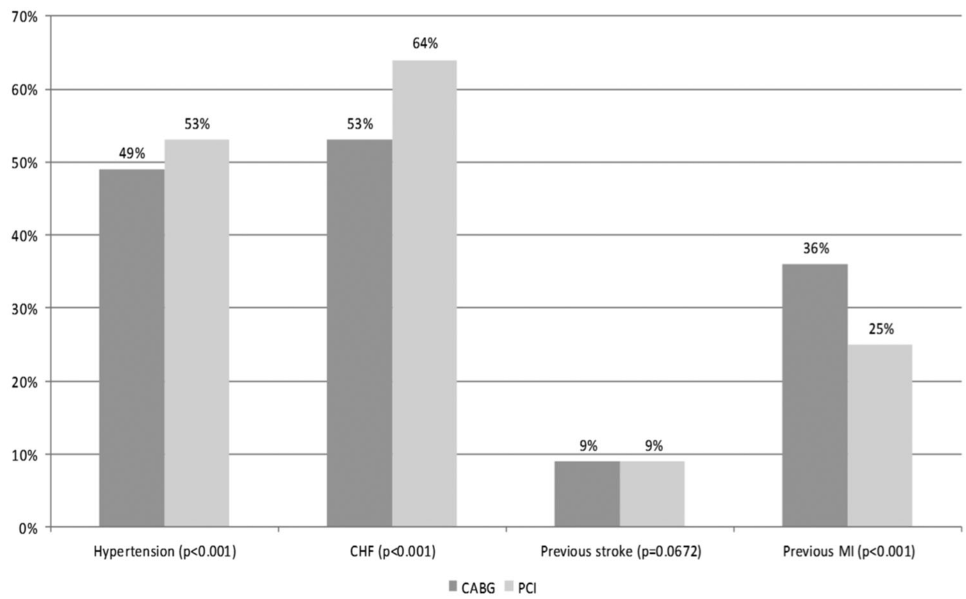

Figure 3. Comorbidity frequencies in diabetic patients undergoing CABG or PCI in Finland in 2000–2015. Adjusted model includes age, gender and region of residence as covariates. CHF: chronic heart failure; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.

Table 3. Odds ratios (OR) for CABG versus PCI among revascularized diabetic patients in 2012–2015.

Characteristic	OR (95% CI)	*p*-Value
Age	1.00 (1.00–1.00)	Ns
Year of the operation	0.92 (0.92–0.93)	<.001
Women	0.74 (0.71–0.78)	<.001
Urgent revascularization	0.70 (0.66–0.74)	<.001
History of MI	2.58 (2.42–2.75)	<.001
History of Stroke	1.06 (0.97–1.15)	Ns
Prevalent AF	0.81 (0.76–0.88)	<.001
Prevalent CHF	0.42 (0.40–0.45)	<.001
Hypertension	0.91 (0.87–0.95)	<.001

Odds ratios (OR), and 95% confidence intervals are shown in parentheses. PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; MI: myocardial infarction; CHF: chronic heart failure; AF: atrial fibrillation.

compared to 39.4% ($n = 14,149$) for CABGs and 60.6% ($n = 21,725$) for PCIs in non-diabetic patients ($p < .001$).

Furthermore, the distributions of the urgencies of CABG and PCI procedures differed between diabetic and non-diabetic patients. Urgent PCI was performed more frequently than elective PCI in diabetic patients when compared to non-diabetic patients (61.6 vs. 55.9% for urgent PCI and 38.4 vs. 44.1% for elective PCI; $p = <.001$). In contrast, elective CABG was more frequent than urgent CABG in diabetic as opposed to non-diabetic patients (61.0 vs. 59.6% for elective, and 39.0 vs. 40.4% for urgent CABG in diabetic vs. non-diabetic patients, respectively; $p = .02$; Figure 4).

Discussion

Diabetes is one of the most important CHD risk factors due to the clustering of metabolic disorders, which results in diffuse and rapidly progressing atherosclerosis [13]. Revascularizations are common in these high-risk patients, whose treatment is further complicated by increased surgical risks, comorbidities and medications, resulting in a need for careful decision-making when considering treatment options [14].

Numerous randomised controlled trials comparing CABG to PCI were published during the bare-metal-stent (BMS) era demonstrating that patients with diabetes who had undergone PCI had an increased risk of restenosis and mortality compared to CABG [4]. Drug-eluting stents (DESs) were introduced in the 2000s, and they prompted a re-examination of the results. Especially the new-generation DES's have been proven to lower the risk of restenosis compared to BMS's, hence making an impact on treating diabetic patients with CHD [5–7,15,16]. More recent RCTs comparing CABG to new generation DES suggest that the difference in survival has narrowed between the two treatment options, and DES could be superior to CABG when comparing the risk of stroke [5–7,10]. To finally put this question to rest, the FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multi-Vessel Disease) trial was conducted and published in 2012. This notable trial compared CABG to DES in patients with diabetes and concluded, yet again, that CABG led to lower all-cause mortality, and reduced the risk for repeat MIs and the need of repeat revascularizations in comparison to PCI with DES. However, CABG was complicated by increased rates of stroke when

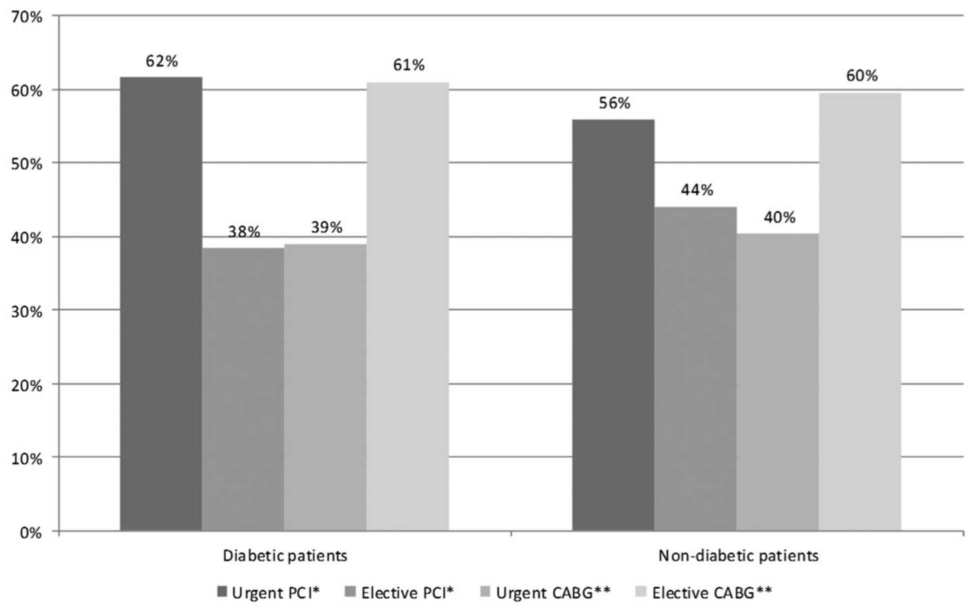

Figure 4. Distribution of urgent versus elective procedures in diabetic patients and non-diabetic patients. Adjusted model includes age and region of residence as covariates. *$p<.001$ (PCI), **$p=.02$ (CABG). PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.

compared to PCI [17]. Further analysis also demonstrated that CABG was more cost-effective compared to PCI [18]. Benefits of CABG over PCI have been confirmed since then in a 2013 meta-analysis combining eight RCTs, four of which are from the modern DES era [19], in 2016 in a pooled analysis of 3 trials evaluating the effect of optimal medical therapy with or without PCI or CABG [20], and again in 2018 in a pooled analysis of 11 randomised trials specifically powered to detect a difference in mortality [3]. The generalizability of the FREEDOM study results has also been proven in a real-world population setting [21].

The impact of the coronary lesion severity on the cardiovascular outcome is still being debated. The treatment of choice for diabetic patients with less complex multi-vessel disease and with two-vessel disease has not been as clear as for those with three-vessel disease, as data are limited in regard to the complexity of coronary anatomy and the completeness of revascularizations. In addition, traditional predictors of revascularization risks, such as fractional flow reserve and Cardiac Surgery (SYNTAX) score, may not be as valuable in this patient group [22,23]. However, in the 2013 ESC guidelines, PCI was already considered as an alternative to CABG in diabetic patients with less complex CHD [1]. Accordingly, the recent 2019 ESC guidelines recommend, that in one or two vessel disease without proximal LAD lesion, PCI is the revascularization method of choice, whereas for patients with DM and multivessel CHD, suitable coronary anatomy for revascularization, and low predicted surgical mortality, CABG is superior to PCI (Class 1 level of evidence) [2].

Our register study evaluating the clinical practice of revascularizations showed that diabetes was associated with increased probability for CABG over PCI. However, the absolute numbers of CABG procedures declined during the study period, and in the last years (2012–2015) constituted only 27% of all revascularization procedures among diabetic patients. PCI was the dominant first revascularization procedure among both diabetic patients and non-diabetic patients. This implies that despite the guidelines favouring CABG, diabetic patients eligible for CABG might receive PCI instead of CABG. This implementation gap has also been identified in previous studies conducted in the BMS era, and more recently by the FREEDOM trial [17,24].

The observed discrepancy in clinical practice patterns is not fully understood. Patients presenting with ST-elevation MI (STEMI) should undergo primary PCI for culprit lesion. When the patient has stabilised, CABG should be performed in case of multivessel disease or disease involving left anterior descending artery (LAD). However, when deciding on revascularization among patients with non-ST-segment elevation myocardial infarction (NSTEMI) and stable coronary artery disease, it has been suggested that physicians' interpretations of the existing evidence demonstrating superiority of CABG over PCI differ [25]. Our register showed that diabetic patients had more urgent CABGs than urgent PCIs when compared to non-diabetic patients. Unfortunately, no data were available of the detailed clinical situation leading to revascularization in our study. Other theories explaining the gap between guideline recommendations and clinical implementation include patient preferences: PCI is less invasive and is known to be more appealing to the patient if no survival advantages are reported by the physician [26]. Differences in local expertise and systems of perioperative care could also alter the decision-making process. Finally, these real world data showed that the revascularization therapy received by Finnish patients with diabetes is not consistent with guideline recommendations. We are further evaluating the magnitude of the possible detrimental effects by comparing outcomes after CABG and PCI in diabetic patients compared to non-diabetic patients in a similar, real-world setting.

Strengths and limitations

A major strength of our study is the large, country-wide electronic register, which includes practically all invasive cardiac procedures performed on diabetic and non-diabetic patients in Finland. The good coverage of the register data has been recently shown and it has been widely used in examining trends in invasive cardiac procedures [12]. Limitations include the administrative nature of the data collection, missing clinical details on risk factors and the extent of the coronary atherosclerosis.

Conclusion

CABG has been performed more frequently in diabetic than in non-diabetic CHD patients. This difference has narrowed over time, and PCI has become the dominant revascularization method in both diabetic and non-diabetic CHD patients. Among diabetic patients, prior MI was associated with increased odds of CABG, whereas other comorbidities and female gender were tilting the balance towards PCI.

Impact on daily practice

Strong evidence suggests that the optimal revascularization method in diabetic patients with CHD is CABG. Nonetheless, PCI is currently the more common method of revascularization. More specific understanding of the benefits and risks of both revascularization strategies will help us optimise treatment for each patient.

Data availability

Due to privacy and legal restrictions, individual-level data used in this article are not available.

Disclosure statement

VS has received honoraria for consultations from Novo Nordisk and Sanofi. He also has ongoing research collaboration with Bayer AG. (All unrelated to the present study.) No potential conflict of interest was reported by the author(s).

Author contributions

H-R L contributed to the study design and the analysis and interpretation of the data and wrote the manuscript. AP contributed to the study design and the analysis and interpretation of the data. TJN, JL and VS contributed to the study design and the analysis and interpretation of the data and provided overall feedback and guidance. All authors revised the manuscript critically for important intellectual content and approved the final version of the manuscript.

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