Treatment variation in stent choice in patients with stable or unstable coronary artery disease

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Abstract

Aim Variations in treatment are the result of differences in demographic and clinical factors (e.g. anatomy), but physician and hospital factors may also contribute to treatment variation. The choice of treatment is considered important since it could lead to differences in long-term outcomes. This study explores the associations with stent choice: i.e. drug-eluting stent (DES) versus bare-metal stents (BMS) for Dutch patients diagnosed with stable or unstable coronary artery disease (CAD).

Methods & results Associations with treatment decisions were based on a prospective cohort of 692 patients with stable or unstable CAD. Of those patients, 442 patients were treated with BMS or DES. Multiple logistic regression analyses were performed to identify variables associated with stent choice. Bivariate analyses showed that NYHA class, number of diseased vessels, previous percutaneous coronary intervention, smoking, diabetes, and the treating hospital were associated with stent type. After correcting for other associations the treating hospital remained significantly associated with stent type in the stable CAD population.

Conclusions This study showed that several factors were associated with stent choice. While patients generally appear to receive the most optimal stent given their clinical characteristics, stent choice seems partially determined by the treating hospital, which may lead to differences in long-term outcomes.
Keywords  Treatment variation · Coronary artery disease · Drug-eluting stent · Bare-metal stent · Percutaneous coronary intervention

Introduction

Despite improvement in the prognosis of patients with cardiovascular disease (CVD) it still remains the second leading cause of death across the Western world and one of the major causes of disability [1]. For many years patients with coronary artery disease (CAD), the most frequent type of CVD, were treated mainly with percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) or medication only. Both revascularisations reduce the incidence of death and myocardial infarction (MI) in CAD patients compared with no treatment, but most patients are now treated with PCI. In 2012 approximately 39,000 PCIs were performed in the Netherlands [2]. Originally a PCI was performed with an expanding balloon; however, nowadays patients are often treated with a bare-metal stent (BMS) or drug-eluting stent (DES). DES reduces restenosis compared with BMS (8.4 versus 20.9 %) [3]. However, patients treated with DES, especially the early-generation, might have a higher chance of developing very late stent thrombosis (0.7 versus 0.1 %) [3]. Both types of stents have pros and cons; decisions should be based on what is considered appropriate for a patient since the choice of stent type may have impact on long-term outcomes. Variations in treatment are the result of differences in patient characteristics and clinical factors (e.g. anatomy) but previous studies have shown that physician and hospital factors may contribute to treatment variation. In the UK, stent choice was associated with the operator and the treating hospital [4]. Tu et al. [5] have shown that the physician performing the diagnostic catheterisation and the treating hospital were strong independent predictors of the type of revascularisation (CABG versus PCI) in Canada. Furthermore, the type of stent was also determined by the type of payer (e.g. Medicaid, private insurance) [6]. Of course, these results may be expected to be healthcare system specific and do not apply for Dutch patients, since the Netherlands has a centrally publicly funded healthcare system.

This study will explore the associations with stent choice (DES or BMS) for Dutch patients diagnosed with stable or unstable CAD focusing on variation due to clinical factors and treating hospital.

Methods

Study design

Treatment variation of patients with stable or unstable CAD was explored through analysing data from the Circulating Cells prospective cohort study, which has the aim of discovering markers that identify patients who are at an increased risk of developing a cardiovascular event. In this multicentre study, patients undergoing coronary angiography were included if they had known or suspected stable or unstable CAD; specific diagnoses included unstable angina and non-ST-elevation MI (NSTEMI) [7].

Treatment

Patients undergoing coronary angiography were asked to participate in the study. Data were collected regarding patient characteristics, test results and treatment decisions. Patients who were treated with a PCI received a BMS, DES, drug-eluting balloon angioplasty or standard balloon angioplasty. The aim of this study is to examine the factors that are associated with stent choice (DES vs. BMS), meaning that patients treated solely with drug-eluting balloon angioplasty or standard balloon angioplasty are excluded from the analyses. Stent choice for DES was defined as a PCI with at least one DES, including patients treated with only DES but also patients treated with DES in combination with BMS, drug-eluting balloon angioplasty or standard balloon angioplasty. Stent choice for BMS was defined as a PCI with only BMS such that patients treated with BMS in combination with balloon angioplasty or DES are excluded.

Data and statistical analyses

Choice of stent type (DES or BMS) was compared between patient subgroups, determined by diagnosis. The following baseline characteristics were also collected during the study: age, gender, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), thrombolysis in myocardial infarction (TIMI) score for unstable CAD patients, New York Heart Association (NYHA) class, number of diseased vessels (50–99 % stenosis), cardiac history (previous heart failure, previous MI, previous PCI, and previous CABG), non-cardiac history (cerebrovascular accident (CVA) or transient ischaemic attack (TIA), pulmonary disease, peripheral vessel disease (PVD), and renal failure), and CVD risk factors (diabetes mellitus, hypertension, hyperlipidaemia, smoking, and pack-years (tobacco)).

Multiple imputation was used to prevent patients from being excluded from the analyses due to missing values. Baseline characteristics (SBP, DBP, BMI, NYHA class, previous heart failure, previous MI, CVA or TIA, pulmonary
Table 1 Baseline characteristics

| Baseline characteristics      | All patients after imputation | Patients with stable CAD | Patients with unstable CAD | p value<sup>a</sup> |
|-------------------------------|-------------------------------|---------------------------|----------------------------|---------------------|
|                              | Mean  | SD   | N<sup>b</sup> | Mean  | SD   | N<sup>b</sup> | Mean  | SD   | N<sup>b</sup> |       |
| Age                           | 62.72 | 10   | 442           | 62.96 | 10   | 358           | 61.71 | 11   | 84           | 0.319  |
| Male (%)                      | 72%   |      |               | 73%   |      |               | 68%   |      |              | 0.354  |
| SBP (mmHg)                    | 135   | 19   | 442           | 135   | 19   | 358           | 134   | 21   | 84           | 0.748  |
| DBP (mmHg)                    | 77    | 11   | 442           | 77    | 11   | 358           | 79    | 11   | 84           | 0.273  |
| BMI (kg/m²)                   | 28    | 4    | 442           | 28    | 4    | 358           | 27    | 4    | 84           | 0.266  |
| TIMI score<sup>c</sup>        |       |      |               |       |      |               |       |      |               |        |
| TIMI score 1                  | 8%    |      | 83            | 8%    |      | 83            |       |      |               |        |
| TIMI score 2                  | 18%   |      | 83            | 18%   |      | 83            |       |      |               |        |
| TIMI score 3                  | 30%   |      | 83            | 30%   |      | 83            |       |      |               |        |
| TIMI score 4                  | 28%   |      | 83            | 28%   |      | 83            |       |      |               |        |
| TIMI score 5                  | 12%   |      | 83            | 12%   |      | 83            |       |      |               |        |
| TIMI score 6<sup>+</sup>7      | 4%    |      | 83            | 4%    |      | 83            |       |      |               |        |
| Number of diseased vessels (50–99%) |       |      |               |       |      |               | 0.077 |      |               |        |
| Number of diseased vessels    |       |      |               |       |      |               |       |      |               |        |
| Number of diseased vessels 1  | 44%   |      | 442           | 46%   |      | 358           | 36%   |      | 84           |        |
| Number of diseased vessels >1 | 56%   |      | 442           | 54%   |      | 358           | 64%   |      | 84           |        |
| NYHA                          |       |      |               |       |      |               |       |      |               |        |
| NYHA I                        | 73%   |      | 442           | 73%   |      | 358           | 76%   |      | 84           |        |
| NYHA II                       | 18%   |      | 442           | 20%   |      | 358           | 7%    |      | 84           |        |
| NYHA III                      | 6%    |      | 442           | 7%    |      | 358           | 4%    |      | 84           |        |
| NYHA IV                       | 2%    |      | 442           | 0%    |      | 358           | 13%   |      | 84           |        |
| Cardiac history (%)           |       |      |               |       |      |               |       |      |               |        |
| Previous heart failure        | 2%    |      | 442           | 2%    |      | 358           | 1%    |      | 84           | 0.542  |
| Previous MI                   | 31%   |      | 442           | 33%   |      | 358           | 23%   |      | 84           | 0.066  |
| Previous PTCA                 | 33%   |      | 442           | 35%   |      | 358           | 26%   |      | 84           | 0.116  |
| Previous CABG                 | 7%    |      | 442           | 8%    |      | 358           | 5%    |      | 84           | 0.369  |
| Non-cardiac history (%)       |       |      |               |       |      |               |       |      |               |        |
| CVA/TIA                       | 8%    |      | 442           | 6%    |      | 358           | 14%   |      | 84           | 0.017  |
| Pulmonary disease             | 11%   |      | 442           | 10%   |      | 358           | 14%   |      | 84           | 0.242  |
| Peripheral vessel disease     | 13%   |      | 442           | 13%   |      | 358           | 14%   |      | 84           | 0.684  |
| Renal failure                 | 3%    |      | 442           | 4%    |      | 358           | 1%    |      | 84           | 0.25   |
| Risk factors (%)              |       |      |               |       |      |               |       |      |               |        |
| Diabetes mellitus             | 21%   |      | 442           | 22%   |      | 358           | 20%   |      | 84           | 0.764  |
| Hypertension                  | 66%   |      | 442           | 67%   |      | 358           | 60%   |      | 84           | 0.189  |
| Hyperlipidaemia               | 68%   |      | 442           | 70%   |      | 358           | 60%   |      | 84           | 0.057  |
| Current smokers               | 19%   |      | 442           | 16%   |      | 358           | 32%   |      | 84           | 0.001  |
| Pack years<sup>d</sup>        | 19.7  | 18   | 442           | 19.2  | 18.1 | 358           | 21.9  | 22.1 | 84           | 0.302  |
| Diagnosis (%)                 |       |      |               |       |      |               |       |      |               |        |
| Stable angina                 | 81%   |      | 442           |       |      |               |       |      |               |        |
| Unstable angina               | 10%   |      | 442           |       |      |               |       |      |               |        |
| NSTEMI                        | 9%    |      | 442           |       |      |               |       |      |               |        |
| Treatment/stent choice        |       |      |               |       |      |               | 0.736 |      |               |        |
| DES                           | 66%   |      | 442           | 66%   |      | 358           | 68%   |      | 84           |        |
| BMS                           | 34%   |      | 442           | 34%   |      | 358           | 32%   |      | 84           |        |
| Hospital                      |       |      |               |       |      |               |       |      |               |        |
| I                             | 29%   |      | 442           | 28%   |      | 358           | 37%   |      | 84           |        |
| II                            | 22%   |      | 442           | 24%   |      | 358           | 13%   |      | 84           |        |
| III                           | 18%   |      | 442           | 14%   |      | 358           | 37%   |      | 84           |        |
| IV                            | 30%   |      | 442           | 34%   |      | 358           | 13%   |      | 84           |        |

BMI body mass index, CABG coronary artery bypass graft, CVA cerebrovascular accident, DBP diastolic blood pressure, MI myocardial infarction, NA not applicable, NSTEMI non ST elevation myocardial infarction, NYHA New York heart association, PTCA percutaneous transluminal coronary angioplasty, SBP systolic blood pressure, TIA transient ischaemic attack, TIMI thrombolysis in myocardial infarction.

<sup>a</sup>Stable versus unstable.

<sup>b</sup>Number of patients on which the analyses were based.

<sup>c</sup>Only reported for unstable angina and NSTEMI.

<sup>d</sup>Number of packs per day multiplied with years of smoking.
In total, 714 patients were included in the Circulating Cells cohort, 22 of whom were excluded from the analyses since they did not have significant coronary atherosclerosis. The remaining 692 patients were included in three teaching hospitals and one general hospital, and 477 patients were treated with PCI. Of those patients, 442 patients were treated with BMS or DES. Others were treated with a combination of BMS and balloon angioplasty \((n=4)\), drug-eluting balloon angioplasty or standard balloon angioplasty \((n=18)\) or missing \((n=13)\) and are excluded from the analysis. The number of patients treated per hospital \((1–IV)\) was 130, 98, 81, and 133, respectively. Table 1 presents the baseline demographic and angiographic characteristics of the included patients. The mean age of the cohort was 63 years and 72% were male. The majority \((81\%)\) of the patients were diagnosed with stable CAD \(n=358)\) and unstable CAD \(n=236)\). There were three significant differences with stable CAD \((including silent ischaemia)\) after the coronary angiography. There were three significant differences in characteristics of stable CAD \((n=358)\) and unstable CAD patients \((n=236)\). Stable CAD patients more often had a lower NYHA class, were less often current smokers and had less often experienced a CVA/TIA compared with unstable CAD patients.

In total, 771 stents were used to treat 442 patients with 612 target lesions. On average, 1.385 target lesions were stented per patient \((range 1–3)\), where 1.260 stents were used per lesion and 1.744 stents \((range 1–6)\) per patient were used. Of the 442 patients, 66% were treated with one or more DES. Bivariate analyses \((Table 2)\) showed that NYHA class, number of diseased vessels, previous PCI, smoking, diabetes and the treating hospital were significantly associated with stent choice for a patient. The frequency of DES use varied widely \((50–99\%)\) between the four hospitals, considering the total population. The variation in stent choice was larger in the unstable patient group \((45–100\%)\).

All multivariate analyses \((Table 3)\) showed that patients with diabetes had a significantly higher chance of receiving DES. The use of DES versus BMS in the stable CAD population was not only associated with diabetes but also with the treating hospital, smoking status, and previous PCI. Patients treated in hospital II or III, patients having diabetes, and patients with a previous PCI had a higher chance of being treated with DES. Patients treated in hospital I and patients who were current smokers had a lower chance of being treated with DES.

Discussion

This study explored the factors associated with stent choice for Dutch patients diagnosed with stable or unstable CAD. Various factors are associated with the frequency of DES use, including diabetes, previous PCI, number of diseased vessels, NYHA class, smoking and the treating hospital.

Patients requiring a PCI were in most cases treated with at least one DES \((66\%)\), which is in line with the guidelines that suggest that patients with stable CAD should receive a DES if there is no contraindication of prolonged dual anti-platelet therapy \([8]\). Furthermore, DES is recommended over BMS in NSTEMI or unstable angina patients with diabetes \([9]\). Since patients with diabetes have a higher restenosis risk than patients without diabetes, DES is considered the most optimal treatment for these patients since DES reduces restenosis compared with BMS. Consequently, diabetes was significantly associated with stent choice in this study. Patients who have been treated before with a PCI were also more likely to receive DES \((76\%)\); these patients have a higher risk of developing restenosis and thus DES was preferred. Patients with multi-vessel disease \((73\%\) DES) and patients with a high NYHA class \((range I–IV: 62–90\%\) DES) were significantly more frequently treated with DES. Studies suggest that patients with multi-vessel disease should be treated with CABG or PCI using DES since these interventions have shown to be more effective than BMS \([10]\). Patients currently smoking were less often treated with DES.

These clinical factors can be considered as legitimate leading to variation in stent choice. However, 19% of the variation in stent choice was explained by these factors in the stable CAD population. Beside clinical factors, other
|                          | All patients |                                   | Patients with stable CAD |                                   | Patients with unstable CAD |
|--------------------------|--------------|------------------------------------|---------------------------|-----------------------------------|----------------------------|
|                          | DES (%)/ OR  | N                                  | p value                   | DES (%)/ OR                      | N                           | p value                   |
| Overall                  | 66%          | 442                                |                           | 66%                               | 358                        |                           |
| Diagnosis                |              |                                    |                           |                                    |                            |                           |
| Stable CAD               | 66%          | 358                                | 0.558                     |                                    |                            |                           |
| Unstable angina          | 63%          | 46                                 |                          |                                    |                            |                           |
| NSTEMI                   | 74%          | 38                                 |                           |                                    |                            |                           |
| Hospital                 |              |                                    |                           |                                    |                            |                           |
|                          | p<0.001      |                                    |                           |                                    |                            |                           |
|                           |             |                                    |                           |                                    |                            |                           |
| 1                        | 50%          | 130                                |                           | 52%                               | 99                         | 45%                       | 31                        |
| 2                        | 64%          | 98                                 | 66%                       | 87                                | 100%                       | 55%                       | 11                        |
| 3                        | 99%          | 81                                 | 98%                       | 50                                | 100%                       | 55%                       | 11                        |
| 4                        | 64%          | 133                                | 65%                       | 122                               | 100%                       | 55%                       | 11                        |
| Baseline characteristics  |              |                                    |                           |                                    |                            |                           |
| Age (years)              | 1.008        | 442                                | 0.387                     | 1.005                             | 358                        | 0.682                     | 1.023                     | 84                        | 0.272                     |
| Gender                   |              |                                    | 0.474                     |                                   | 0.46                        |                            | 0.872                     |
| Male                     | 67%          | 318                                | 67%                       | 261                               | 68%                        | 7                         |                            |                            |
| Female                   | 64%          | 124                                | 63%                       | 97                                | 67%                        | 27                        |                            |                            |
| SBP (mmHg)               | 1.007        | 442                                | 0.188                     | 1.003                             | 358                        | 0.598                     | 1.022                     | 84                        | 0.074                     |
| DBP (mmHg)               | 0.998        | 442                                | 0.815                     | 0.997                             | 358                        | 0.767                     | 1.001                     | 84                        | 0.968                     |
| BMI (kg/m²)              | 1.038        | 442                                | 0.128                     | 1.049                             | 358                        | 0.08                       | 0.994                     | 84                        | 0.912                     |
| TIMI score              |              |                                    | 0.085                     |                                   |                            |                            |                           |
|                          |              |                                    |                           |                                    |                            |                           |
| 1                        | 71%          | 7                                  | 71%                       |                                   | 7                          |                           |                           |
| 2                        | 80%          | 15                                 | 80%                       |                                   | 25                         |                           |                           |
| 3                        | 48%          | 25                                 | 48%                       |                                   | 25                         |                           |                           |
| 4                        | 83%          | 23                                 | 83%                       |                                   | 23                         |                           |                           |
| 5                        | 60%          | 10                                 | 60%                       |                                   | 10                         |                           |                           |
| 6+7                      | 100%         | 3                                  | 100%                      |                                   | 3                          |                           |                           |
| NYHA                     |              |                                    |                            |                                    | 0.036                       | 0.011                     |
| NYHA I                   | 62%          | 324                                | 63%                       | 260                               | 59%                        | 64                        |                            |                            |
| NYHA II                  | 71%          | 79                                 | 69%                       | 73                                | 100%                       | 6                         |                            |                            |
| NYHA III & IV           | 90%          | 39                                 | 88%                       | 25                                | 93%                        | 14                        |                            |                            |
| Number of diseased vessels |              |                                    |                            |                                    |                            | 0.102                     |
| 1                        | 58%          | 196                                | 58%                       | 166                               | 57%                        | 30                        |                           |                            |
| >1                       | 73%          | 246                                | 72%                       | 192                               | 74%                        | 54                        |                            |                            |
| Cardiac history          |              |                                    |                            |                                    |                            |                           |
| Previous heart failure   |              |                                    |                            |                                    |                            |                           |
| Yes                      | 67%          | 9                                  | 63%                       | 8                                 | 100%                       | 1                         | 0.489                     |
| No                       | 66%          | 433                                | 66%                       | 350                               | 67%                        | 83                        |                            |                            |
| Previous MI              |              |                                    |                            |                                    |                            |                           |
| Yes                      | 72%          | 137                                | 72%                       | 118                               | 74%                        | 19                        |                            |                            |
| No                       | 64%          | 305                                | 63%                       | 240                               | 66%                        | 65                        |                            |                            |
| Previous PTCA            |              |                                    |                            |                                    |                            |                           |
| Yes                      | 76%          | 148                                | 76%                       | 126                               | 77%                        | 22                        |                            |                            |
| No                       | 61%          | 294                                | 60%                       | 232                               | 65%                        | 62                        |                            |                            |
| Previous CABG            |              |                                    |                            |                                    |                            | 0.433                     |
| Yes                      | 61%          | 31                                 | 63%                       | 27                                | 50%                        | 4                         |                            |                            |
| No                       | 67%          | 411                                | 66%                       | 331                               | 69%                        | 80                        |                            |                            |
| Non-cardiac history      |              |                                    |                            |                                    |                            |                           |
| CVA/TIA                  |              |                                    |                            |                                    |                            |                           |
| Yes                      | 69%          | 35                                 | 70%                       | 23                                | 67%                        | 12                        | 0.924                     |
| No                       | 66%          | 407                                | 66%                       | 335                               | 68%                        | 72                        |                            |                            |
| Pulmonary disease        |              |                                    |                            |                                    |                            | 0.445                     |
| Yes                      | 56%          | 47                                 | 55%                       | 35                                | 58%                        | 12                        |                            |                            |
| No                       | 68%          | 395                                | 36%                       | 323                               | 69%                        | 72                        |                            |                            |
After adding treating hospital to the regression analysis 33% of the variation in stent choice could be explained. The analyses showed that the frequency of DES use ranged from 50–99% of all patients across hospitals. This difference could result from a difference in patient case mix, despite the adjustment for many individual patient characteristics in the analyses. Furthermore, payment arrangements with stent manufacturers and budget constraints may have influenced the stent choice. Another potential reason, patient preference, could have influenced the variation in stent choice. However, we expect this to be minimal since both interventions can be considered to be equally invasive.

Implications

In general, patients receive the most optimal stent given their clinical characteristics. However, stent choice is also determined by the treating hospital, probably due to operator variation and availability and supply of resources. Variation should only occur due to demographic and angiographic factors. When variation is due to factors other than demographics or angiography findings it could lead to less optimal stent choices and subsequently differences in long-term outcomes.
Table 3  Multivariate analyses therapeutic decision (BMS vs DES)

|                  | Bivariate analyses (OR) | Multivariate analyses (OR) | \( p \) value* |
|------------------|-------------------------|----------------------------|----------------|
| **Total population (\( n = 442 \))** |                         |                            |                |
| Number of diseased vessels       |                         |                            |                |
| 1                              | 0.520                   | 0.560                      | 0.006          |
| >1                             | Ref                     |                            |                |
| NYHA class                  |                         |                            |                |
| NYHA class I                 | Ref                     |                            |                |
| NYHA class II                | 1.478                   |                            |                |
| NYHA class III+IV            | 5.311                   |                            |                |
| Hospital                      |                         |                            |                |
| 1                             | 0.565                   |                            |                |
| 2                             | 1.016                   |                            |                |
| 3                             | 45.176                  |                            |                |
| 4                             | Ref                     |                            |                |
| Diabetes (yes vs no)          | 8.680                   | 8.318                      | \(<0.001\)     |
| Renal artery disease (yes vs no) | 0.368               |                            |                |
| Current smoker (yes vs no)    | 0.599                   |                            |                |
| Previous MI (yes vs no)       | 1.486                   |                            |                |
| PVD (yes vs no)               | 1.017                   |                            |                |
| Previous PTCA (yes vs no)     | 2.045                   |                            |                |
| TIMI score*                   |                         |                            |                |
| 1                             | Ref                     |                            |                |
| 2                             | 1.20                    |                            |                |
| 3                             | 0.37                    |                            |                |
| 4                             | 2.000                   |                            |                |
| 5                             | 0.600                   |                            |                |
| 6+7                           | 646189937               |                            |                |
| Constant                      |                         | 1.911                      | \(<0.001\)     |
| Nagelkerke R\(^2\)           |                         | 16%                        |                |
| Stable CAD (\( n = 358 \))    |                         |                            |                |
| BMI (kg/m\(^2\))             | 1.049                   |                            |                |
| Hospital                      |                         |                            |                |
| 1                             | 0.578                   | 0.466                      | 0.013          |
| 2                             | 1.034                   | 1.047                      | 0.884          |
| 3                             | 26.671                  | 29.381                     | 0.001          |
| 4                             | Ref                     | Ref                        |                |
| Previous MI (yes vs no)       | 1.513                   |                            |                |
| NYHA class                    |                         |                            |                |
| NYHA class I                  | Ref                     |                            |                |
| NYHA class II                 | 1.280                   |                            |                |
| NYHA class III+IV             | 4.319                   |                            |                |
| Number of diseased vessels    |                         |                            |                |
| 1                             | 0.536                   |                            |                |
| >1                            | Ref                     |                            |                |
| Current smoker (yes vs no)    | 0.588                   | 0.404                      | 0.014          |
| Diabetes (yes vs no)          | 8.454                   | 12.001                     | \(<0.001\)     |
| Previous PTCA (yes vs no)     | 2.103                   | 2.284                      | 0.003          |
| Constant                      | 1.207                   |                            | 0.397          |
| Nagelkerke R\(^2\)           |                         | 33%                        |                |
| Unstable CAD (\( n = 84 \))   |                         |                            |                |
| Hospital                      |                         |                            |                |
| 1                             | 0.686                   |                            |                |
| 2                             | 1.000                   |                            |                |
| 3                             | 1346229036              |                            |                |
| 4                             | Ref                     |                            |                |
Patients receiving DES have a lower risk of target lesion revascularisation than patients treated with BMS [3]. However, there is some concern of late stent thrombosis that may occur more frequently after DES than BMS [3]. Besides the implications of treatment variation on the effectiveness, it is also important to consider the costs. While BMS is less expensive than DES, BMS leads to more reinterventions than DES. Several studies have estimated the cost-effectiveness of DES versus BMS and many of these studies concluded that initial DES treatment was overall more expensive than the BMS strategy [12–23]; the reduction in reinterventions did not offset the initial higher stent costs. In most of the studies DES was slightly more effective [12–23] often leading to an incremental cost-effectiveness ratio that could not be considered cost-effective [13, 14, 17, 18, 23]. However, some specific subgroups (diabetes, complex lesions, complex vessels, multi-vessel disease, or a combination of these risk factors) were identified in which DES resulted in a higher health gain in terms of quality-adjusted life-years compared with subgroups that were not at high risk of restenosis and complications. Consequently, in these subgroups, DES was considered more cost-effective. In our study some of these specific subgroups were also associated with a more frequent use of DES.

Limitations

The factors examined in the analyses explained 13–33% of the variation in treatment decisions. While the treating hospital was associated with stent choice, it is possible that hospital is a proxy for a pre-existing patient case mix. Many clinical factors were included in the regression models but it is possible that factors that are of predictive value were not included. Furthermore, the underlying reason why the treating hospital is associated with stent choice is unknown. This could be due to the operator (e.g. experience), for which data were not available for our analyses, or the availability and supply of resources might explain the association with the treating hospital, even though the Netherlands has a centrally publicly funded healthcare system.

We were not able to compare patients treated solely with BMS and patients treated solely with DES. Stent choice for DES was defined as a PCI with at least one DES which includes patients treated with only DES but also patients treated with DES in combination with BMS, drug-eluting balloon angioplasty or standard balloon angioplasty. Consequently, the associations that we have found actually explain why some patients receive DES and why other patients did not receive DES.

In addition, this study did not take into consideration the differences in stent choice (different types of DES) despite variation in their effectiveness. For example, the newer ultra-thin strut BMS leads to less restenosis than the thicker strut BMS; a study using the SOLSTICE registry showed that ultra-thin strut BMS leads to low 6-month major adverse cardiac event rates (5.8%), including target lesion revascularisations [24]. Furthermore, we made no distinction between the types of drug coating (e.g. paclitaxel, sirolimus, or everolimus) used for DES, even though this may affect clinical outcomes.

Lastly, the latest guideline on myocardial revascularisation [25] concluded that the newer generation DES have improved safety outcomes including death, MI and stent thrombosis compared with early-generation DES and BMS.
During this study, this guideline was not available and thus it is possible that stent choice might have been somewhat different if the new guidelines had been applicable; DES could be more frequently used. Furthermore, we did not focus on fully bioresorbable stents, which have promising clinical outcomes since they provide desirable transient vessel support without compromising the restoration of normal vessel biology, vessel imaging or treatment options in the long run [26]. Consequently, the stents evaluated in the Circulating Cells cohort may not reflect the stent choices that will be made in the near future.

Recommendations

This study showed the existence of treatment variation across hospitals that may have an impact on long-term outcomes. It would be interesting to investigate if the treatment variation seen in this cohort will actually lead to differences in long-term outcomes and costs, which could be achieved by increasing the follow-up period. Van der Sijde et al. [27] have also emphasised the role of clinical observations to determine the most appropriate indication for specific types of stents.

Conclusions

This study showed that several clinical factors were associated with stent choice (DES or BMS) for CAD treatment, including diabetes, smoking, NYHA class, multi-vessel disease and previous PCI. In general, it appears that patients receive the most optimal stent given their clinical characteristics. After correcting for the clinical factors, stent choice was also associated with the treating hospital probably due to operator variation and the availability and supply of specific stent types. These differences may lead differences in long-term outcomes.

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Conflicts of interest The authors have no conflicts of interest to declare.

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