Research Article

Outcomes of Drug-Eluting Stents in comparison to Bare Metal Stents in Cancer Patients with Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis

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Background. Studies have demonstrated poor prognosis in cancer patients who undergo percutaneous coronary intervention (PCI) for coronary artery disease (CAD). Cancer patients receiving PCI are at increased risk of in-stent thrombosis, bleeding, hospital readmissions, and cardiovascular and noncardiovascular mortality when compared to patients without cancer. It is unclear if the poor outcomes in cancer patients are related to the stent type utilized for PCI. This meta-analysis attempts to identify differences in efficacy and safety outcomes when comparing drug-eluting stents (DESs) with bare metal stents (BMSs) in cancer patients. Methods. This meta-analysis is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines. Medline, Scopus, and Cochrane Central Register of Controlled Trials were systematically searched to identify relevant studies. Risk of bias was assessed using the Modified Newcastle-Ottawa scale and Cochrane risk of bias tool. The primary outcomes of interest were in-stent thrombosis, bleeding, and mortality. Results. Four studies comprising of 54,414 patients met the inclusion criteria. There was no difference in in-stent thrombosis (odds ratio (OR): 0.79; 95% confidence interval (CI): 0.58–1.07), bleeding events (OR: 1.38; 95% CI: 0.77–2.49), or in-hospital mortality (OR: 1.92; 95% CI: 0.83–4.43) when comparing cancer patients who underwent PCI with DES vs BMS. Conclusions. This meta-analysis demonstrates no difference in mortality, bleeding, or in-stent thrombosis between revascularization with BMS vs DES in patients with cancer and CAD. Cancer patients included in this meta-analysis experienced higher rates of mortality, bleeding, and in-stent thrombosis after PCI compared to all-comers described in the literature.

1. Introduction

Cardiovascular disease and cancer are the two leading causes of death in the United States [1]. As medical therapies have advanced and mortality related to both cancer and cardiovascular disease has declined, these conditions are now more frequently encountered concomitantly, leading to a new specialist field termed Cardio-Oncology [2]. In addition, cardiovascular disease and cancer share many risk factors leading to increased comorbidity prevalence including obesity, smoking, alcohol use, sedentary lifestyle, diet, and chronic inflammation [3]. One area of interest is in the treatment of coronary artery disease (CAD) and acute coronary syndrome (ACS) among patients with cancer. ACS has a poor prognosis among cancer patients including those who undergo percutaneous coronary intervention (PCI) [4–6]. Patients with cancer are at elevated risk of both cardiovascular and noncardiovascular mortality and complications relative to those without cancer [7, 8]. Recent studies have shown that patients with cancer were more likely to have both bleeding and stent thrombosis than those undergoing PCI [7, 9]. Cancer patients are also more likely to be readmitted to the hospital within thirty days of PCI [6]. Reasons for these poor outcomes are multifactorial.
including chemotherapy-induced thrombocytopenia, hypercoagulability, and, if gastrointestinal cancer is present, increased substrate for bleeding [10, 11]. Though there are many reasons why patients with cancer have an increased risk of complications and mortality, it is unclear whether coronary stent type has any impact on outcomes in cancer patients. Though guidelines recommend twelve months of dual antiplatelet therapy (DAPT) following an ACS event regardless of stent type, bare metal stents (BMSs) endothelialize more quickly and clinicians may be more comfortable discontinuing DAPT earlier in order to reduce the bleeding risk in patients with cancer [12, 13]. Alternatively, it has been shown that malignancy causes an increased risk of in-stent thrombosis and drug-eluting stents (DESs) may be beneficial as these have lower rates of in-stent thrombosis [14, 15]. Clearly, there is a need to determine the best stent type for patients with cancer. The primary aim of this meta-analysis is to determine if stent type affects mortality, in-stent thrombosis, or bleeding complications among patients with cancer undergoing PCI for CAD.

2. Methods

2.1. Data Sources and Search Strategy. This systematic review and meta-analysis is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines [16]. Medline, Scopus, and Cochrane Central Register of Controlled Trials were searched from database inception through January 2023 using the following combination of keywords: coronary artery disease OR heart disease OR CAD OR coronary disease OR acute coronary syndrome OR myocardial infarction AND stent OR bare metal stent OR drug eluting stent AND cancer OR malignancy OR tumour. Article language was restricted to English. We also searched trial registries, https://www.clinicaltrialresults.org, https://www.clinicaltrials.gov, abstracts, and presentations from major cardiovascular proceedings. All citations retrieved from the search were transferred to EndNote X7.5 Reference Manager (Thompson ISI ResearchSoft, Philadelphia, Pennsylvania) and duplicates were removed.

2.2. Study Selection. All citations were screened by one reviewer (MUS). Eligible studies reported on outcomes in cancer patients who underwent percutaneous revascularization for coronary artery disease with DES compared to BMS. We included randomized and nonrandomized studies. Exclusion criteria included studies that focused on percutaneous treatment for coronary artery disease in cancer patients without studying the effects of treatment strategy on outcomes. Main outcomes of interest were in-stent thrombosis, in-hospital mortality, and bleeding events.

2.3. Data Extraction and Risk of Bias. Two independent reviewers (MUS and EW) extracted the data on year of publication, study design, inclusion criteria, primary endpoints, and follow-up time using a standardized data extraction form. Risk of bias was assessed using the Modified Newcastle-Ottawa scale for observational studies, which assesses 3 domains: patient selection, comparability, and outcome assessment [17]. For randomized controlled trials (RCTs), Cochrane risk of bias tool was utilized [18]. The methodological quality of a study was graded as high or low based on whether the study had adequate adjustment for confounders [19].

2.4. Statistical Analysis and Certainty in the Estimates. We extracted or calculated an odds ratio (OR) and 95% confidence intervals (CI) from each study. Relative risks were pooled using a random effect model to account for between study variance [20]. The I²-statistic was quantified to measure heterogeneity with values >25%, 50%, and 75% consistent with low, moderate, and high degrees of heterogeneity, respectively [21]. Review Manager Software v5.4 was used for analysis. p values less than 0.05 were considered statistically significant. Certainty in the evidence (i.e., confidence in the final estimates) was assessed using the GRADE approach (Grades of Recommendation, Assessment, Development, and Evaluation) based on the risk of bias, imprecision, indirectness, inconsistency, and publication bias [22].

3. Results

3.1. Study Selection. Of 524 potential articles screened, four studies comprising of 54,414 patients with cancer were included (Figure 1) [7, 23–25]. Of these, 23,817 patients underwent revascularization with BMS and 30,597 patients with DES. The studies did not separate first- and second-generation DES in their analysis and reported their results together. Three studies included all-comers for PCI (ACS and stable CAD) and one study only included stable CAD. However, none of the studies differentiated ACS from stable CAD and results were reported as all-comers for PCI. All studies were observational (nonrandomized). Table 1 summarizes the characteristics of the included studies. Table 2 summarizes the baseline characteristics of included patients. The data on gender are not reported in 2 studies; therefore, we are unable to identify the number of males/females included in this study. Mean age of the patients who underwent revascularization with BMS and DES was 70.6 years and 70.2 years, respectively. Mean follow-up duration was 8.2 years. Table 3 shows the risk of bias assessment. There was high risk of selection bias and performance bias in the four observational studies given the lack of randomization and blinding. Overall, the risk of detection bias, reporting bias, and attrition bias was low among all the studies. We were unable to statistically evaluate publication bias due to the small number of included studies.

When comparing cancer patients with coronary artery disease who underwent revascularization using BMS compared to those who were revascularized with DES, three studies reported stent thrombosis outcomes and the pooled result did not identify any significant difference in risk of stent thrombosis (OR: 0.79; 95% CI: 0.58–1.07) (Figures 2 and 3). Two studies reported in-hospital mortality and found...
no significant difference when the results were pooled (OR: 1.92; 95% CI: 0.83–4.43) (Figure 3). Two studies reported bleeding complications and on pooling the results found no difference between patients with CAD who received revascularization with BMS vs DES (OR: 1.38; 95% CI: 0.77–2.49) (Figure 4).

3.2. Certainty in the Estimates. The included studies were observational, with variable methodological quality and increased risk of selection and confounding bias. The estimates were not precise for the three reported outcomes given a smaller number of events. There was no indirectness or evidence of publication bias. Heterogeneity was noted among the included studies. The quantified I² values for each individual outcome investigated are as follows: in-stent thrombosis (16%) (none), in-hospital mortality (98%) (high), and bleeding complications (96%) (high). Overall, the certainty in the estimates in all the outcomes was judged to be low.

4. Discussion

4.1. In-Stent Thrombosis. In this meta-analysis of 54,414 patients with cancer, there was no significant difference in mortality, bleeding events, or in-stent thrombosis between DES and BMS placement. Overall, this study’s rates of in-stent thrombosis were high relative to the published literature with 146 events (3%) in BMS patients and 251 events (5%) in DES patients. Even with early generation DES, in-stent thrombosis rates are usually reported to be much lower with one large study showing only 61 events (1%) out of 8,146 patients [26]. This is consistent with the literature in that, regardless of stent type, patients with cancer are more likely to have thrombotic events and are at higher risk for in-stent thrombosis [14, 27].

There have been various proposed mechanisms for increased thrombosis risk in patients with cancer including the proinflammatory nature of cancer leading to inappropriate activation of the clotting cascade and platelet aggregation. For example, cancer procoagulant is a cysteine protease found in 81% of patients with cancer that has been shown to
### Table 1: Characteristics of included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Experimental arm</th>
<th>Control arm</th>
<th>Endpoints</th>
<th>Follow-up duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al. [24]</td>
<td>Single-center retrospective cohort study</td>
<td>Cancer patients who underwent PCI using BMS or DES</td>
<td>PCI using BMS</td>
<td>PCI using DES</td>
<td>Stent thrombosis</td>
<td>2 years 10 months</td>
</tr>
<tr>
<td>Munawar et al. [23]</td>
<td>Retrospective cohort study</td>
<td>Patients with concomitant diagnosis of cancer undergoing PCI between January 2004 and December 2014 were identified in the National Inpatient Sample</td>
<td>PCI using BMS</td>
<td>PCI using DES</td>
<td>In-hospital mortality and stent thrombosis</td>
<td>10 years</td>
</tr>
<tr>
<td>Guo et al. [7]</td>
<td>Retrospective cohort study</td>
<td>Cancer patients undergoing PCI at Mayo Clinic Rochester from January 1, 2003, to December 31, 2013</td>
<td>PCI using BMS</td>
<td>PCI using DES</td>
<td>All-cause mortality, MI, and revascularization rate</td>
<td>10 years</td>
</tr>
<tr>
<td>Potts et al. [25]</td>
<td>Retrospective cohort study</td>
<td>Patients undergoing PCI between January 2004 and December 2014 were identified in the National Inpatient Sample</td>
<td>Patients with current/previous cancer undergoing PCI</td>
<td>Patients without current/previous cancer undergoing PCI</td>
<td>In-hospital mortality, bleeding, and stroke</td>
<td>10 years</td>
</tr>
</tbody>
</table>

BMS, bare metal stent; DES, drug-eluting stent.
directly activate factor X [28]. It is present in solid and hematologic tumours but not in normal tissue and is able to activate the coagulation cascade in the absence of factor VII amplification. Scialla et al. highlighted how patients with cancer experience increased platelet surface sialyltransferase activity leading to accelerated thrombosis [29]. In addition, cancerous tissue shed microparticles that interact with P-selectin and further activate platelet aggregation leading to increased incidence of thrombus formation [30]. In-stent thrombi tend to be platelet-rich [31] and associated with enhanced activation of the intrinsic coagulation cascade with concomitant down-regulation of Protein C [32], both of which are seen in malignancy. Together, these factors likely contribute to the higher rates of in-stent thrombosis seen in our cancer patient cohort compared to all-comers who undergo PCI.

Regarding in-stent thrombosis in the general population, a large study including 9,013 patients found that rates of revascularization within six years of PCI were lower in patients who received DES compared to BMS (hazard ratio, 0.76; 95% CI, 0.69 to 0.85; p < 0.001) [33]. This suggests that DES may be preferred over BMS in patients with cancer who have a higher risk of thrombosis; however, our meta-analysis suggests that DES and BMS had similar rates of in-stent thrombosis. Current guidelines include a Class 1 recommendation for a minimum of one month of DAPT after BMS placement and six months of DAPT after DES placement in the setting of stable CAD [34]. Further research is required to determine the optimal duration of DAPT after PCI in patients with cancer.

4.2. Bleeding Complications. Bleeding rates were higher than reported in the literature with 2,324 events (10%) in the BMS cohort and 1,797 events (6%) in the DES cohort in this meta-analysis. According to the HMO Research Network-Stent Registry including 8,137 patients (including those with and

Table 2: Patient baseline characteristics.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Group</th>
<th>Gender</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>F</td>
<td>Both</td>
<td>Mean</td>
</tr>
<tr>
<td>Ahmed et al. [24], 2022</td>
<td>BMS</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DES</td>
<td>N/A</td>
<td>N/A</td>
<td>304</td>
</tr>
<tr>
<td>Munawar et al. [23], 2022</td>
<td>BMS</td>
<td>3037</td>
<td>1276</td>
</tr>
<tr>
<td>DES</td>
<td>3049</td>
<td>1264</td>
<td>4313</td>
</tr>
<tr>
<td>Guo et al. [7], 2021</td>
<td>BMS</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DES</td>
<td>N/A</td>
<td>N/A</td>
<td>290</td>
</tr>
<tr>
<td>Potts et al. [25], 2019</td>
<td>BMS</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DES</td>
<td>N/A</td>
<td>N/A</td>
<td>25,690</td>
</tr>
</tbody>
</table>

Table 3: Risk of bias assessment of the included observational studies.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Comparability</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Adjustment</td>
<td>Unadjusted</td>
<td>Adjusted</td>
<td>Unadjusted</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Outcome</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total (maximum score = 9)</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

For selection, the highest score was 4 based on the representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of the exposure, and outcome of interest at the start of the study; for comparability, the highest score was 2 based on comparability of the cohort; and for outcome, the highest score was 3 based on assessment of the outcome, follow-up period, and adequacy of the follow-up.

![Figure 2: Forest plot for in-stent thrombosis comparing revascularization with BMS and DES in cancer patients with coronary artery disease.](image-url)
without malignancy) who underwent PCI, 4.8% of patients experienced a bleeding-related hospitalization after discharge [35]. The international multicenter registry ADAPT-DES prospectively followed 8,556 patients who underwent PCI with a DES and found that 6.2% of patients experienced a bleeding event that required medical attention [36]. The increased risk of bleeding in patients with cancer has been extensively documented in the literature and has been attributed to a multitude of factors including chemotherapy side effects as well as factors intrinsic to malignancy including excessive fibrinolysis, decreased coagulation factor production, thrombocytopenia, bone marrow failure, metastasis, acquired hemophilia, and von Willebrand deficiency [37–39]. These factors in combination with DAPT put patients with cancer at high risk of bleeding after PCI.

Multiple scoring systems have been developed in an attempt to predict which patients will be at high risk of bleeding; however, there is no consensus on the best tool for patients with cancer requiring DAPT after PCI. The PRECISE-DAPT calculator was developed in 2017 and can be used to predict the risk of out-of-hospital bleeding while on DAPT [40] (calculator can be found in reference [41]). It considers five clinical parameters including the patient’s hemoglobin, age, white blood cell count, creatinine clearance, and history of prior bleed to categorize patients as high or low bleed risk. This information can help guide physicians to determine optimal DAPT duration. More recently, the Academic Research Consortium for High Bleeding Risk (ARC-HBR) created a more comprehensive scoring system composed of eleven major criteria and six minor criteria [42]. According to this scoring system, a patient is deemed high bleed risk if they fulfill at least one major and two minor criteria. While the ARC-HRB may provide a more tailored risk assessment, it is yet to be validated using a prospective patient cohort. In efforts to balance the risks of in-stent thrombosis and bleeding complications, the MASTER DAPT trial compared the outcomes of one-month vs  

Figure 3: Outcomes of drug-eluting stents in comparison to bare metal stents in cancer patients with percutaneous coronary intervention (figure created with https://BioRender.com).
In hospital mortality

Subtotal (95% CI) 23649
Potts 2019
Munawar 2022
Heterogeneity: $\tau^2 = 0.36$; $\chi^2 = 49.30$, Total events 1204 634

Test for overall effect: $Z = 1.08$ ($P = 0.28$)

Bleeding complications

Subtotal (95% CI)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>BMS Events</th>
<th>Total</th>
<th>DES Events</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Munawar 2022</td>
<td>203</td>
<td>4313</td>
<td>164</td>
<td>4313</td>
</tr>
<tr>
<td>Potts 2019</td>
<td>1001</td>
<td>19336</td>
<td>470</td>
<td>25690</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>23649</td>
<td>30003</td>
<td>100.0</td>
<td>49.4</td>
</tr>
<tr>
<td>Total events</td>
<td>1204</td>
<td>634</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.17$; $\chi^2 = 24.01$, Total events 1204 634

Test for overall effect: $Z = 1.08$ ($P = 0.28$)

**Figure 4:** Forest plot for in-hospital mortality and bleeding complications comparing revascularization with BMS and DES in cancer patients with coronary artery disease. The pooled risk ratio with 95% confidence interval was calculated using a random effects model. Weight refers to the contribution of each study to the pooled estimate. Squares and horizontal lines denote the point estimate and 95% confidence interval. BMS, bare metal stent; DES, drug-eluting stent.

standard three-month DAPT duration after PCI [43]. It found that one-month DAPT was noninferior to three-month DAPT regarding number of major cardiac/cerebral events and superior at reducing the number of bleeding events. This suggests that in high-risk patients with cancer, physicians may consider reducing the duration of DAPT without adversely impacting MACE outcomes.

4.3. Mortality. Rates of in-hospital mortality in this meta-analysis were high with 1,204 events (5%) and 634 events (2%) within the BMS and DES groups, respectively. A large randomized controlled trial including 8,404 patients found the 30-day mortality after PCI in all comers to be 1.6% [44]. This is in congruence with Nakatsuka et al. who found that patients with a history of cancer had a higher five-year mortality after PCI than patients without cancer [45]. This is likely due to a combination of bleeding and increased rates of thrombosis among patients with cancer. Complications from cancer and its treatments likely contribute to in-hospital and overall mortality as well.

Given that there was no difference in in-stent thrombosis, bleeding, or mortality in this meta-analysis, these outcomes are less likely to be modified by stent type. It follows that anticoagulation, DAPT duration, and postprocedural and postdischarge management are likely to have the greatest impact on long-term outcomes rather than stent type and this requires further research.

4.4. Limitations. The limitations of this study are primarily due to paucity of literature on the topic. There was heterogeneity in the baseline characteristics of the patients included in each study which may have hindered analysis. Additionally, all the included studies were observational in design and lacked randomization, which increases the possibility of selection and confounding bias. Due to lack of gender data in the individual studies, we were unable to identify any differences in outcomes based on gender. The included studies did not stratify DES generation, limiting the ability to specifically compare outcomes between second-generation DES and BMS. This meta-analysis only investigated rates of in-stent thrombosis and did not examine in-stent restenosis rates. This requires further investigation as the increased risk of in-stent restenosis with BMS is a common deterrent in all patient populations. Finally, as most of the included articles are retrospective studies based on chart review, DAPT compliance is unknown which could greatly influence the analyzed outcomes in bleeding, in-stent thrombosis, and mortality.

5. Conclusions

In this meta-analysis including 54,414 patients, there was no difference in mortality, bleeding, or in-stent thrombosis between BMS and DES in cancer patients with CAD. Cancer patients included in this meta-analysis experienced higher rates of mortality, bleeding, and in-stent thrombosis after PCI compared to all-comers described in the literature. This is likely due to increased bleeding and thrombosis seen in patients with cancer as well as the proinflammatory nature of malignancy. There are multiple validated calculators to predict the severity of bleed risk in patients with cancer which can help inform optimal DAPT duration in high-risk patients. This meta-analysis showed no difference in outcome between DES and BMS, so physicians should treat patients based on individualized risk-benefit profiles and focus on DAPT duration and postprocedural and postdischarge management to optimize cancer patient outcomes after PCI.

**Data Availability**

Data are safely kept in a password protected security system at Thomas Jefferson University Hospital. The datasets used and/or analyzed during the current study are deidentified and available from the corresponding author on reasonable request.
Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. As this was a meta-analysis, this study did not require approval by our institutional review board. This article does not contain any studies with animals performed by any of the authors.

Disclosure

The results presented in this paper have not been published previously in whole or part, except in abstract form at the Journal of the Society for Cardiovascular Angiography & Interventions in May 2023.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

MS, EW, and JJ were responsible for data collection, analysis, and manuscript preparation. PO, DS, EK, and MM were responsible for analysis and manuscript preparation. DF was responsible for design, manuscript preparation, and supervision.

References


[21] R. M. Turner, J. Davey, M. J. Clarke, S. G. Thompson, and J. P. Higgins, “Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane Database of


