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EDITORIAL COMMENT

The Pros and Cons of Percutaneous Coronary Intervention in Patients With Cancer*

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As cancer survivorship increases, patients with cancer are living longer, leading to increasing amounts of time to manifest the sequelae of coronary artery disease. Similarly, with improvements in the management and treatment of coronary artery disease, patients are living long enough with atherosclerosis to subsequently develop cancer. As such, there has been a steady rise in the frequency of percutaneous coronary intervention (PCI) performed in patients with cancer (1). However, patients with concomitant cancer and coronary artery disease pose unique clinical challenges to both cardiologists and oncologists. Many cancers adversely affect the coagulation cascade. Also, the therapies required for various cancers can increase risks of bleeding and/or thrombosis. These considerations lead to areas of uncertainty with regard to PCI, with valid concerns arising both about stent performance and appropriate post-PCI antithrombotic therapy in this unique population.

To this end, Ueki et al. (2) provide an important contribution to this field in this issue of the *JACC: CardioOncology*. The authors performed an analysis of the Bern PCI registry, which contains detailed clinical and follow-up information on >13,000 patients that underwent PCI at a large medical center in Switzerland. They found that 10% of PCI patients had a historical diagnosis of cancer with a wide variety of cancer types. Among these patients, 9% had metastatic disease and 13% were undergoing active therapy for cancer at the time of PCI. More than 90% of patients were on dual antiplatelet therapy, with roughly 10% of patients on triple antithrombotic therapy (dual antiplatelet plus anticoagulant therapy) at the time of discharge. Using a propensity-matched cohort analysis, the authors discovered that patients with cancer who underwent PCI had an increase in major bleeding (hazard ratio [HR]: 1.55; 95% confidence interval [CI]: 1.14 to 2.11; $p = 0.005$) but no difference in major ischemic events (HR: 1.18; 95% CI: 0.93 to 1.50; $p = 0.181$) at 1 year. Patients with cancer who underwent PCI had a significantly increased risk of all-cause death at 1 year (HR: 2.03; 95% CI: 1.55 to 2.65; $p < 0.001$). Finally, patients undergoing PCI with a recent cancer diagnosis (<1 year from diagnosis) experienced higher risks of both bleeding and cardiac death.

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The results of this study highlight 2 main points regarding the care of patients with cancer who require PCI. First, it is noteworthy that in a cohort of patients almost universally treated with modern generation drug-eluting stents, there was not an increased incidence of stent-related complications in patients with cancer. Specifically, rates of stent thrombosis and target vessel revascularization were similar between patients with and without cancer in the propensity-matched analysis. These findings are salient because cardiovascular surgeons are often reasonably hesitant to operate on patients with cancer, typically because

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of concerns of long-term prognosis. The results of this study support the contention that PCI is a safe and viable option among cancer patients to treat unstable coronary syndromes and can also be considered as an option to relieve angina and improve quality of life in select circumstances.

Second, patients with cancer have an elevated bleeding risk after PCI. The Academic Research Consortium for High Bleeding Risk recently released a consensus document that highlighted active malignancy as a major criterion for assessing bleeding risk (3). This signal for increased bleeding risk among cancer patients who undergo PCI is remarkably consistent among a variety of studies, with a 1-year major bleeding rate of 5% to 10%. The LEADERS FREE (A Randomized Clinical Evaluation of the Bio-Freedom Stent) trial found a BARC (Bleeding Academic Research Consortium) 3 to 5 bleeding rate of 9.6% within 1 year among a subset of patients with cancer who underwent PCI, and the Trilogy-ACS trial found a GUSTO (Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries) moderate/severe/life-threatening bleeding rate of 11.2% (4,5). The current study by Ueki et al. (2) found a 5.8% risk of BARC 3 or 5 bleeding at 1-year in patients with cancer. The major bleeding rates from these studies are in contrast to rates under 5% in most studies of patients without cancer. Thus, although stents may perform well in patients with cancer, these patients remain at high risk of bleeding post-PCI because of the cancer, its associated treatments, and the antithrombotics necessary after cardiac intervention.

Thus, it becomes paramount to identify strategies to modify bleeding risk in this high-risk population. One such strategy may be to reduce the use of potent P2Y12 inhibitors (prasugrel and ticagrelor) in favor of clopidogrel. In the cohort studied by Ueki et al. (2), 30% of patients with cancer received treatment with a potent P2Y12 inhibitor. Although prasugrel and ticagrelor reduce the rate of ischemic events after PCI in patients who present with acute coronary syndrome, this comes at the cost of an increased bleeding risk (6,7), and the bleeding risk may be accentuated in patients with cancer. This population represents an attractive target for research in tailored therapy using CYP2C19 genotyping. A recent trial demonstrated the safety of de-escalation of antiplatelet therapy among a broad group of patients with ST-segment elevation myocardial infarction when normal clopidogrel metabolism was confirmed via genotyping (8).

Further, it appears particularly important to minimize the use of triple antithrombotic therapy in these patients. In the current study, patients with cancer were more likely to be on an anticoagulant compared with patients without cancer (11.4% vs. 7.9%; $p < 0.001$), and the rate of triple antithrombotic therapy was also higher (12.3% vs. 8.2%; $p < 0.001$). Though largely untested in the cancer population, novel studies have examined varying combinations of oral anticoagulants with antiplatelet agents to minimize bleeding risk for patients with atrial fibrillation who undergo PCI (9). Combinations of direct oral anticoagulants with antiplatelet monotherapy may be particularly attractive among patients with cancer who undergo PCI that require concomitant anticoagulation.

Finally, more research is needed regarding abbreviated dual antiplatelet therapy durations among post-PCI cancer patients. This high-bleeding risk population that exhibits good technical stent performance represents a logical and attractive option for shorter dual antiplatelet regimens. Recent trials have investigated the risks and benefits of short duration dual antiplatelet therapy with largely positive results (10–13), though patients with malignancy have largely been excluded from such efforts. It remains to be seen if there is an ischemic risk to be paid in the cancer population with shorter dual antiplatelet regimens.

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