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ORIGINAL ARTICLE

Incidence, Predictors and Outcomes of Major Bleeding in Patients Following Percutaneous Coronary Interventions in Australia

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Background Major bleeding is a serious complication of percutaneous coronary intervention (PCI). We set out to investigate the incidence of major bleeding and its impact on hospitalisation and long-term mortality.

Method We examined seven years of registry data encompassing 16,860 PCI procedures.

Results Between 2005 and 2011 major bleeding increased from 1.3% to 3.4%. In patients with ST elevated myocardial infarction (STEMI), the rate increased from 2.3% to 6.4%. The increase remained significant after adjusting for patient and procedural characteristics (OR=1.09/year, p=0.001). Bleeding risk was highest in patients presenting with out-of-hospital cardiac arrest and cardiogenic shock (CS). Women, STEMI patients, those aged over 70yrs or weighing <60 kg were at higher risk. Glycoprotein IIb/IIIa-inhibitor use more than doubled the risk of bleeding (OR=2.28, p=<0.001). Mortality rates at one year were 4.18% overall and 7.9% in STEMI. Bleeding was a strong predictor of mortality after adjusting for potential confounders (HR=2.92, 95% CI: 2.08, 4.09). Bleeding significantly increased length of stay (med four days vs seven days) and rehospitalisation at 12 months (OR=1.36, 95% CI: 1.08, 1.70).

Conclusions Major bleeding rates post-PCI appear to be increasing in Australia. Bleeding increases hospitalisation and is associated with poor clinical outcomes.

Keywords Percutaneous coronary intervention • Bleeding • Hospitalisation • Mortality • PCI • STEMI

Introduction

Bleeding is a common complication of PCI that not only has an immediate impact on the well-being of the patient and the need for additional resources in hospital, but also contributes to poor long-term outcomes including increased risk of death [1–8]. The risk of bleeding is likely to depend on the individual risk profile of the patient being treated, the

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interventions undertaken and the anti-coagulant regimens being used [5,9,10].

Since there is a trade-off between avoiding ischaemic events and avoiding bleeding, knowing the risks for bleeding events and the outcomes following bleeding can help target strategies to reduce the incidence of bleeding [9–11].

In this study we present the incidence, predictors and outcomes of bleeding following PCI in a cohort of Australian patients from the Melbourne Interventional Group (MIG) registry.

Methods

Study Population

We undertook a retrospective analysis of MIG Registry data comprising 16,860 PCI procedures from six major Victorian hospitals between 2005 and 2011. Human Research Ethics Committee approval was sought and obtained. Details of participation and data collection have been published previously. In brief, baseline demographics, clinical, angiographic, and procedural characteristics of consecutive patients undergoing PCI are prospectively recorded on case report forms using standardised definitions for all fields [12]. The protocol has been approved by the ethics committee in each participating hospital, including the approval for the use of ''opt-out'' consent [13–15].

In-hospital outcomes and complications were recorded at the time of discharge. Follow-up was undertaken at 30-days and 12-months, either by telephone or record review, using a standardised questionnaire [12–15]. Clinical events were validated by reviewing medical records, where available.

The registry is coordinated by the Centre for Cardiovascular Research & Education in Therapeutics, a research body within the Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia. An independent audit is conducted annually at all enrolling sites by an investigator not affiliated with that institution. A number of verifiable fields from 5% of all procedures entered from each site annually are randomly selected and audited. In the most recent audit undertaken, 27 fields were reviewed and data accuracy was 98%, which is comparable to other large registries [15,16].

Clinical Endpoints

A major bleeding complication was defined as any bleed that occurred during or after the catheter laboratory visit until discharge, and required a transfusion, and/or prolonged the hospital stay, and/or caused a drop in haemoglobin > 3.0 gm/dl. This definition is similar to the major bleed definition used in major trials [17–19].

Bleeding site was categorised as percutaneous entry site, retroperitoneal, or 'other', which includes gastrointestinal, genital or urinary, other sites, or unknown.

Time-to-death was defined as the difference between the procedure date and the date of death up to 365 days. Length of stay was defined as the difference between date of admission and date of discharge from admitting hospital (or date of death). Readmissions to hospital were recorded for patients who survived the initial hospitalisation up to one year after discharge, including the primary readmission reason.

Statistical Analysis

Logistic regression was used to identify predictors of bleeding and re-admission to hospital. Cox models were used to evaluate the effect of bleeding on length of stay in hospital and mortality. SAS software, version 9.3 was used for all analyses.

Candidate variables (including age, sex, co-morbidities, disease type, procedure characteristics and anti-coagulation strategies) were initially evaluated in univariate models. Variables which were statistically significant ($p<0.05$) were included in a multivariate model. Backward selection was used to select variables significant at the $p<0.1$ level for the final models. Two-way interactions were included if the p-value for the interaction was less than 0.01. There was evidence that the mortality risk from bleeding differed in CS patients. Since CS was an extremely strong predictor of mortality we ran separate models for CS and non-CS patients.

Results

A total of 16,860 procedures from six hospitals were included in the analysis. Baseline characteristics are shown in Table 1. The mean age at the time of procedure was 64.6±11.9 years and three-quarters of the patients were male. Clinically, 28% of the cohort presented with STEMI, with a further 37% presenting with NSTEACS.

Major bleeding occurred in 2.4% of the procedures. 38.9% of bleeds were at the percutaneous entry site, 8.3% were retro-peritoneal and the remaining 46.5% were classified as 'other'. Among patients with an out-of-hospital cardiac arrest (OHCA), only 10% (4/40) of bleeds were located at the percutaneous entry site. Thirty-three per cent (132/405) of bleeds required a blood transfusion. Five per cent (22/405) of bleeds were associated with a pseudo-aneurysm and four of these required surgery. Bleeding rates increased significantly during the study period (Table 2). Bleeding rates were highest in older patients and females. Patients presenting with chronic stable angina had the lowest rates of bleeding (1.2%) while the highest rates were in patients presenting with STEMI (4.4%). Bleeding and mortality rates for co-morbidities and anticoagulant treatments are shown in Table 3. Procedural characteristics are summarised in Appendix 2.

Factors Associated with Bleeding

Age, gender, weight, OHCA, cardiogenic shock (CS), glycoprotein IIb/IIIa-inhibitor (GPI) use, and ACS type were found to be predictive of bleeding complications (Table 4).

The risk of bleeding was lowest in 50-69 year-olds. The rates were higher in patients under 50 and those over 70. The interaction between OHCA and gender was significant.