Retroperitoneal Bleeding after Cardiac Catheterization: A 7-Year Descriptive Single-Center Experience

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Abstract

Background: Retroperitoneal bleeding (RPB) is an unusual but potentially fatal vascular complication occurring after cardiac catheterization (CC). Contemporary data of RPB in the era of dual antiplatelet therapy and vascular closure devices are lacking. Methods: We retrospectively examined all RPB cases that occurred after CC in the Rabin Medical Center between the years 2005 and 2011. Results: Of 26,487 patients who underwent CC, a total of 48 patients (mean age 60.9 ± 13.8 years, 52.1% female) with RPB were identified (0.18%). The indication for CC was acute coronary syndrome (43.7%), myocardial infarction (35.4%), stable angina pectoris (8.3%), hemodynamic studies for valvular heart disease (10.4%) and others (2.1%). Coronary intervention was performed in 34 patients (70.9%) and a vascular closure device (VCD) was used in 16 patients (33.3%). Seventy-seven percent of patients were treated with clopidogrel, 20.8% with glycoprotein IIb-IIIa inhibitors and 85.4% with anticoagulation during CC. Median time to diagnosis of bleeding was 9.0 h, while the median time to bleeding differed between patients with and without a VCD (12 vs. 5 h, respectively). The clinical presentation of RPB was hemorrhagic shock in 39.6% of patients and 50.0% required at least one blood transfusion. Patients were managed either with conservative treatment (79.2%), angiography stenting (14.6%) or vascular surgery (6.2%). A total of 3 patients died during hospitalization, of which RPB was the etiology in 2 (4.2%). Conclusions: RPB which is a rare complication of CC is associated with younger age and female gender, as compared to patients without RPB. Onset of bleeding can be delayed in patients with VCDs. With careful and early diagnosis, most patients with RPB after CC can be managed conservatively.

Introduction

Cardiac catheterization (CC) is performed for diagnostic or therapeutic purposes in over 3 million patients annually in 2,100 laboratories in the United States alone [1]. Recent national and international guidelines sup-
port an expanding role of CC with a wide range of indications [2]. Despite the high-volume nature of this procedure, vascular post-CC complications remain common. In fact, bleeding represents the most common complication of percutaneous coronary interventions (PCI) occurring in 5.5% of all patients and is associated with over USD 10,000 added medical costs to the care episode [3]. Retroperitoneal bleeding (RPB) is an unusual but potentially fatal vascular complication occurring after CC [4–6]. Current data regarding the clinical characteristics and management of RPB in the era of newer CC procedures, the use of dual antiplatelet therapy and the use of vascular closure devices (VCD) are lacking. We therefore aimed to examine the incidence, characteristics and management of RPB in the era of contemporary CC procedures.

Methods

We retrospectively examined all CC procedures with femoral access that were performed in the Rabin Medical Center between January 2005 and November 2011 (n = 26,487). We identified all cases of RPB using the CC database and patient medical records. Clinical, procedural and in-hospital outcomes were based on the institutional database and when necessary on the patient medical records. Patients who underwent CC due to transcutaneous aortic valve replacement, ventricular septal defect and atrial septal defect were not included in the present analysis.

We have also examined the database for the 26,439 patients without RPB. The only variables that were available for further analysis were age, gender and the urgency of catheterization and these characteristics were compared to RPB patients. The selection and disposition of the RPB cohort is summarized in figure 1.

Procedural Details

PCI was performed according to the standard guidelines. Briefly, coronary angiography was undertaken using standard interventional techniques with femoral access. The standard size of femoral sheaths used for diagnostic angiography and PCI was 6 Fr. All patients received unfractionated heparin to goal activated clotting time of 225–300 s or with bivalirudin, per operator preference. In high-risk patients without specific bleeding-related contraindications, glycoprotein (GP) IIb-IIIa inhibitors were added. VCD were used depending on the clinical scenario and the patient vascular anatomy. The VCDs used were Angioseal (St. Jude Medical), Perclose proglide (Abbott vascular) and exoseal (Cordis). Standard manual compression or Femostop compression assist devices (St. Jude Medical) were otherwise used. Femoral sheath was removed 4–6 h after the CC in the cardiology intensive care or intermediate units. The patient was advised to remain in supine position for at least 4 h after a diagnostic procedure and at least 12 h after therapeutic PCI. Hemorrhagic shock was defined as systolic blood pressure ≤90 mm Hg. Chronic renal failure (CRF) was defined as a glomerular filtration rate of less than 60 ml/min/1.73 m², based on the Cockcroft-Gault formula. Postprocedurally, all patients received aspirin 100 mg daily and a daily ADP antagonist. The choice of ADP antagonist was left to operator discretion with the use of
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clopidogrel 300 or 600 mg loading dose followed by 75 mg daily. Dual antiplatelet therapy was continued for at least 6 months in the majority of patients. Prasugrel and ticagrelor were not yet used in our institute in the study period.

Statistical Analysis
Clinical variables included in this analysis were normally distributed (verified by the Kolmogorov-Smirnov test). All results are presented as the mean ± SD for continuous variables and as percentage of total patients for categorical data. Two-sided Student’s t-tests were used for comparison of the continuous variables and χ² tests and Fischer exact tests for categorical data, as appropriate. Statistical analysis was performed by using STATISTICA software (StatSoft Inc., Tulsa, Okla., USA), and p < 0.05 was considered significant for all analyses.

Results
Of the 26,487 patients who underwent CC with femoral access, a total of 48 patients (mean age 60.9 ± 13.8 years, 52.1% female) with RPB were identified (overall prevalence 0.18%). A comprehensive description of patient characteristics is presented in table 1.

Baseline Characteristics
The indication for CC was acute coronary syndrome (43.7%), myocardial infarction (35.4%), stable angina pectoris (8.3%), hemodynamic studies for valvular heart disease (10.4%) and right heart catheterization (2.1%). The mean BMI of the patients with RPB was 24.6 ± 3.4. Twelve patients had diabetes mellitus (25.0%), 1 had peripheral vascular disease (2.1%) and 3 patients (6.3%) had CRF. Seven patients were treated with warfarin while only 4 had an international normalized ratio >1.8 prior to the CC. Similarly, only 1 patient had evidence of thrombocytopenia prior to the CC.

As compared to patients without RPB (n = 26,439), baseline characteristics that were less associated with RPB were male gender (OR 0.3, 95% CI 0.13–0.65, p = 0.002) and age >60 years (OR 0.3, 95% CI 0.14–0.70, p = 0.004).

Procedural Characteristics
Coronary intervention was performed in 34 patients (70.9%). Of this group, 23 patients (67.6%) had a PCI of a single vessel and the rest had a 2-vessel PCI. Anticoagulation during CC was used in 41 patients (85.4%) of which 39 patients were treated with unfractioned heparin and 2 patients with bivalirudin. The mean dose of heparin used during the PCI was 5,330 ± 2,600 IU. Seventy-seven percent of the patients were treated with clopidogrel and 20.8% with GP IIb-IIIa inhibitors (eptifibatide).

Vascular Closure Devices
VCD was used in 16 patients (33.3%), in particular Angioseal (13 cases). The median time to bleeding was 9.0 h, while it differed between patients with and without a VCD (12 vs. 5 h, respectively). Most cases of RPB in patients without VCD occurred during the first 8 h after CC while in patients with VCD, the time interval to bleeding was up to 72 h after CC. The time intervals from CC to RPB are depicted in figure 2.

Diagnosis and Management
The clinical presentation of RPB was abdominal pain in 91.7% of the patients and hemorrhagic shock was present in 39.6% of patients. The diagnosis of RPB was established in most cases by computed tomography (93.8%). Half of the patients had received blood transfusion during hospitalization. Patients were managed conservatively in the majority of cases (79.2%), but angiography stenting (14.6%) or vascular surgery (6.2%) was required in a substantial proportion. Of the patients who required interventional treatment (n = 9), 7

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Table 1. Baseline characteristics of patients with RPB (n = 48)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>60.9±13.8</td>
</tr>
<tr>
<td>Female</td>
<td>25 (52.1)</td>
</tr>
<tr>
<td>BMI</td>
<td>24.6±3.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (25.0)</td>
</tr>
<tr>
<td>Renal insufficiency (GFR &lt;60 ml/min)</td>
<td>3 (6.3)</td>
</tr>
<tr>
<td>PVD</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Indication for CC</td>
<td></td>
</tr>
<tr>
<td>Acute MI</td>
<td>17 (33.3)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>17 (35.4)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>21 (43.7)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>4 (8.3)</td>
</tr>
<tr>
<td>Prior to valve surgery</td>
<td>5 (10.4)</td>
</tr>
<tr>
<td>Right heart catheterization</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Preprocedural platelets, ×10^3/μl</td>
<td>243.5±74.4</td>
</tr>
<tr>
<td>Preprocedural INR &gt;1.8</td>
<td>4 (8.3)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>37 (77.1)</td>
</tr>
<tr>
<td>Heparin</td>
<td>39 (81.2)</td>
</tr>
<tr>
<td>Glycoprotein IIb-IIIa inhibitors</td>
<td>10 (20.8)</td>
</tr>
<tr>
<td>PCI</td>
<td>34 (70.9)</td>
</tr>
<tr>
<td>One vessel</td>
<td>23 (67.6)</td>
</tr>
<tr>
<td>Two vessel</td>
<td>11 (32.4)</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>VCD placement</td>
<td>16 (33.3)</td>
</tr>
</tbody>
</table>

Values are mean ± SD, or n (%).
GFR = Glomerular filtration rate; INR = international normalized ratio; MI = myocardial infarction.
were women (77.8%), 8 patients (88.9%) had a systolic blood pressure below 90 mm Hg, 4 patients (44.4%) were treated with warfarin, all patients received blood transfusions and none were treated with VCDs. In 1 case, angiography and stenting was followed by surgery after 48 h due to ongoing bleeding. A total of 3 patients died during the index hospitalization of which RPB was the etiology in 2 patients (4.2%) with a mean time from CC to death of 27 h. The third case of death was due to bacteremia and sepsis, irrespective to the RPB (table 2).

**Gender Differences**

Females with RPB were older than males (68.0 ± 14.2 vs. 51.7 ± 9.8 years, respectively, p < 0.001) and were treated less commonly with GP IIb-IIIa inhibitors and VCD placement (7.7 vs. 36.3%, p = 0.03 and 19.2 vs. 50.0%, p = 0.02, respectively).

**Discussion**

We examined a contemporary large cohort of patients with RPB after CC and found a relatively low prevalence of RPB (0.18%) despite concomitant treatment with dual antiplatelet therapy and heparin in the majority of patients. These findings are consistent with the historical reported incidence of RPB after CC, which varies considerably across studies in the last 2 decades ranging from 0.1 to 3.0% [4–6]. This variation could reflect recent advancements in PCI technique, disparities in operator experience, novel antithrombotic regimens and the emergence of VCD.

Our study emphasizes the difference in RPB characteristics in patients with and without VCD and the important differences between men and women who develop RPB after CC. Several risk factors for the development of RPB after CC have been previously identified including female gender, low BMI, CRF, high femoral puncture site and the use of GP IIb-IIIa inhibitors [7–12]. Indeed, the majority of patients with RPB in our cohort were female but only few had a low BMI or CRF. Interestingly, a number of gender differences were observed in our study. Younger age and female sex were associated with RPB as compared to patients without RPB. However, in the group of patients who developed RPB, women were older than men. Furthermore, although similar rates of PCI procedures were performed in men as compared to women, women were less frequently treated with GP IIb-IIIa inhibitors. In fact, women may have a slightly higher rate of major and minor bleeding rates with GP IIb-IIIa inhibitors infusions [7, 8, 11]. Furthermore, VCDs were used mainly in men; this finding could be explained by the smaller arterial dimension in women which could limit the use of VCDs [13].
VCDs are commonly used in the contemporary era as a primary method of closure of vascular access. The association of VCD and RPB remains controversial, but recent meta-analyses show no difference in access-related complications between VCDs and manual compressions [14, 15]. VCDs were used in one third of the patients in our cohort (most commonly the Angioseal closure device). RPB which developed in patients with VCD was delayed and appeared even after 72 h following CC. Although VCD use may result in a perception of low risk of bleeding, this finding emphasizes the need for higher clinical suspicion for RPB in patients with VCD even several days after the procedure.

The most serious complication of RPB after CC is death. The mortality rate in our study was 4.2% which is concordant with previous reports [16]. Half of the patients in our cohort have received blood transfusion, a treatment that although relatively safe, is an independent predictor for short and long term mortality and therefore should be administered appropriately [16]. Indeed, most cases of RPB in our cohort were managed conservatively by clinical evaluation, close laboratory follow-up and by administering blood transfusion as needed. Angiography and stenting rather than vascular surgery were more commonly used in our cohort as compared to previous reports [5, 17], which may be related to the evolution and development of newer angiographic techniques for vascular closure in recent years. According to our results, patients who required interventional treatment were mostly females who were admitted with low BP and none were treated with VCDs. Due to small number of patients, we cannot conclude what are the factors associated with the need for interventional treatment in RPB patients and future research is needed.

**Limitations**

There are several notable limitations to the current investigation. First, It is a retrospective analysis based on a single center experience, still it is unique in its long-term clinical follow-up and it represents the experience of a single tertiary medical center in consecutive patients referred for CC. Secondly, the study population is heterogeneous since it includes patients who underwent coronary angiography for different etiologies, as well as right heart catheterizations. Data on patients without RPB were missing and therefore we cannot deduce conclusions regarding all the predictors associated with RPB. Data on the procedure time, arterial sheath width, location of vascular puncture and hospital stay were lacking in the institutional database. No data were available regarding all patients who had abdominal pain after CC who did not undergo evaluation for RPB. Still, in our institute, abdominal pain after CC mandates ruling out RPB as an etiology.

**Conclusions**

Based on a large, single-center contemporary cohort, RPB is a rare complication of CC. Younger age and female gender is associated with RPB. Time to onset of bleeding can be delayed in patients treated with VCD. With careful and early diagnosis, most patients with RPB after CC can be managed conservatively.

**Disclosure Statement**

There are no potential sources of conflict for this research.

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**References**


