Anti-Platelet Therapy: No Association with Increased Blood Loss in Patients Undergoing Open or Laparoscopic Appendectomy

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ABSTRACT: **Background:** The effect of anti-platelet drugs on surgical blood loss and perioperative complications has not been studied in depth and the management of surgical patients taking anti-platelet medications is controversial.

Objective: To assess the effect of anti-platelet therapy on perioperative blood loss in patients undergoing appendectomy either laparoscopically or via open surgery.

Methods: We reviewed the files of all patients › 40 years old who underwent open or laparoscopic appendectomies from 2007 to 2010. Excluded were patients with short hospitalization and no follow-up of hemoglobin level, patients on warfarin treatment and patients who underwent additional procedures. Estimation of blood loss was based on decrease in hemoglobin level from admission to discharge. Risk factors for blood loss, such as anti-platelet therapy, age, gender, surgical approach, surgical time, surgical findings and complications, were analyzed.

Results: The final cohort included 179 patients (mean age 61 ± 14 years, range 40–93) of whom 65 were males. The mean perioperative hemoglobin decrease was 1.59 ± 1.07 mg/dl (range 0–5 mg/dl). Thirty-nine patients received anti-platelet therapy prior to surgery and 140 did not. No significant differences in decrease of hemoglobin level were found between patients receiving anti-platelet therapy and those who were not (1.73 ± 1.21 vs. 1.55 ± 1.02 mg/dl, $P = 0.3$). In addition, no difference was found between patients on anti-platelet therapy operated laparoscopically and those operated in an open fashion (1.59 ± 1.18 vs. 2.04 ± 1.28 mg/dl, $P = 0.29$). Five patients required blood transfusions, two of whom were on anti-platelet therapy. Blood loss was significantly greater in patients with a perforated appendicitis and in those with an operative time of more than one hour.

Conclusions: Anti-platelet therapy does not pose a risk for increased blood loss following emergent appendectomy performed either laparoscopically or in an open fashion.

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Acetylsalicylic acid (aspirin) is an anti-platelet drug used for primary and secondary prevention of cardiovascular and cerebrovascular events. Aspirin inhibits COX enzymes, thus abolishing TxA_2 production in platelets and interfering with their ability to aggregate. Its use has proven effective in the prevention of vascular events, but it is also associated with bleeding, mostly in the gastrointestinal tract [1,2]. Clopidogrel is another potent anti-platelet drug of the thienopyridine group that inhibits ADP receptors. It is considered superior to aspirin for secondary prevention following cardiovascular events, it is widely administered following cardiac catheterization and stent implantation or bypass, and its indications are expanding [1,2].

These two anti-platelet drugs are used widely and the question of their influence on perioperative bleeding tendency is frequently raised. Appendectomy for acute appendicitis is one of the most common surgical procedures performed worldwide. This condition is a progressive infectious process that eventually leads to perforation and, therefore, early surgical intervention and appendectomy is advocated for source control [3]. Both the laparoscopic and traditional open surgical techniques are used. Some authors have demonstrated that the laparoscopic approach reduces hospital stay and postoperative pain and enables the patient's early return to work [4-6]. As with other surgical interventions, appendectomy may be associated with some degree of blood loss reflected in a drop in hemoglobin levels. More rarely, a significant blood loss may lead to cardiovascular complications, mainly in the older age groups [1].

The aim of this study was to assess the effect of anti-platelet therapy on perioperative blood loss in patients over 40 years old undergoing an appendectomy. We hypothesized that anti-platelet therapy (clopidogrel and/or aspirin) might increase the amount of perioperative blood loss.

PATIENTS AND METHODS

A list of all patients over 40 years old who underwent appendectomy in the Tel Aviv Sourasky Medical Center between January 2007 and March 2010 was generated from the insti-

tute's database. The patients' data were collected retrospectively from medical charts. Inclusion criteria were age above 40 years and first-time appendectomy by either laparoscopy or an open approach. Exclusion criteria were concomitant performance of other surgical procedures, insufficient information in the medical records, and preoperative use of warfarin.

The primary outcome was perioperative blood loss, which was estimated based on the difference between hemoglobin concentration at admission to hospital and postoperative hemoglobin concentration levels. Investigated factors included anti-platelet treatment, surgical approach (open surgery or laparoscopic), patient's age and gender, intraoperative findings (perforation, abscess), length of operative time, postoperative complications, and length of hospital stay.

STATISTICAL ANALYSIS

Statistical analysis for continuous and categorical parameters was performed using the Student's *t*-test. A multivariate linear regression model was used for multivariate analysis. A P value ≤ 0.05 was considered significant.

RESULTS

A total of 531 patients met the primary inclusion criteria. Only 190 patients had follow-up hemoglobin levels postoperatively. Of these patients, three who were receiving warfarin treatment and eight who underwent additional surgical procedures concomitantly with the index operation were excluded. The remaining 179 patients comprised the study group. The mean patient age was 61 ± 14 years (range 40–93) and 65 of them were males (36%).

Seventy-eight patients were operated laparoscopically and 101 patients via an open approach. Mean operation time was 65 ± 26 minutes (range 18–181). The appendix was found to be perforated in 40 patients (22%). Mean hospital stay was 6.4 ± 4.4 days (range 1–33). Postoperative complications occurred in 42 patients and included surgical wound complications (infection, delayed closure; n=12), periappendicular abscess formation (n=13), bowel obstruction or ileus (n=9), and other complications (fever, deep vein thrombosis, pulmonary embolism, gastrointestinal bleeding; n=8).

The mean decrease in hemoglobin level following the operation was 1.62 ± 1.05 (0–5 mg/dl). Thirty-nine patients received anti-platelet treatment (8 clopidogrel, 31 aspirin) and 140 did not. No significant difference was found in the decrease in hemoglobin level between patients receiving anti-platelet treatment (1.73 ± 1.21 mg/dl) and those without anti-platelet treatment (1.55 ± 1.02 mg/dl, $P = 0.3$) and between patients treated with clopidogrel (1.15 ± 1 mg/dl) and those treated with aspirin (1.97 ± 1.22 mg/dl, $P = 0.09$). Among patients receiving anti-platelet therapy, no significant difference was found in the decrease in hemoglobin level between patients who were operated laparoscopically (12 patients, 1.59 ± 1.18 mg/dl) and those who were operated via an open approach (27 patients, 2.04 ± 1.28 mg/dl, $P = 0.29$). Five patients required blood transfusions, two of whom were on anti-platelet therapy (not significant).

A linear regression model assessing factors that may be associated with increased blood loss, such as anti-platelet therapy, gender, age, surgical approach (laparoscopy or open), perforated appendicitis and operative time, revealed that blood loss was significantly greater among patients with a perforated appendicitis ($P = 0.005$) and among those with an operative time of more than one hour ($P = 0.024$). Age, gender and other postoperative complications (abscess formation, wound infection or delayed closure, vein thrombosis, pulmonary embolism, fever, respiratory complications) were not associated with significantly greater blood loss.

DISCUSSION

Anti-platelet agents are commonly used as primary and secondary prevention for cardiovascular disease. The question of withdrawing these drugs prior to elective operations is frequently raised. A large meta-analysis on the impact of low-dose aspirin on surgical blood loss demonstrated an increased risk for intraoperative bleeding by a factor of 1.5 [7]. However, increased bleeding was associated with specific procedures [7]. Surgical procedures that have been associated with increased blood loss and increased complication rate when performed on patients receiving anti-platelet therapy included endoscopic large polyp resection [8,9], hip arthroplasty [10], transbronchial biopsy [11], tonsillectomy [12], transurethral prostatectomy [7,13,14], and neurosurgical procedures [15]. With these procedures increased bleeding may lead to significant complications due to anatomic considerations (i.e., closed spaces, impending airway obstruction). Other procedures, such as simple endoscopy [16-18], cardiothoracic surgery [19-21], internal fixation of femoral neck fracture [22,23] and spinal instrumentation and fusion surgery [24], were not associated with a substantial increase in blood loss and related complications.

We did not find specific reports relating to the effect of anti-platelet treatment on blood loss in abdominal operations. Since acute appendicitis is an indication for emergent surgical intervention, the question of anti-platelet drug withdrawal is irrelevant in this setting. Therefore, we thought that appendectomy can serve as a model to evaluate bleeding risk in intra-abdominal surgery in patients taking anti-platelet drugs.

Blood loss in appendectomy is usually mild and estimated surgical bleeding is not often reported by the surgeon. As a result, we chose to look at the perioperative drop in hemoglobin levels as an expression of estimated blood loss. Hemoglobin changes may be influenced by other factors;

however, we believe that in these surgical settings it may serve as a rough measure for blood loss. We have clearly shown that anti-platelet therapy was not a significant risk factor for increased blood loss, as reflected in the decrease in hemoglobin level.

In this study several patients were excluded because of short hospitalization and the absence of follow-up of hemoglobin level. We believe that this fact increases the significance of our results as the patients who were included probably had a longer and more complicated course that potentially may be associated with greater blood loss.

Our results are consistent with previously mentioned reports on operations in other sites when no closed and limited spaces are involved [16-24]. We believe that our findings may serve as additional evidence for the continuation of anti-platelet therapy in patients undergoing elective abdominal surgery associated with mild to moderate bleeding.

Chassot et al. [25] have suggested an algorithm regarding discontinuation of anti-platelet drugs prior to elective operations. In this algorithm the risks for cerebrovascular and cardiovascular complications are combined with the surgical hemorrhagic risk. According to this algorithm, aspirin and clopidogrel should be maintained in operations of mild and moderate hemorrhagic risk even in the low-risk patient.

Another question that was addressed in our study was the impact of the surgical approach on bleeding risk. We found no correlation between surgical approach (open vs. laparoscopic) and bleeding risk in patients on anti-platelet treatment. Thus, the issue of anti-platelet therapy does not have to influence the decision on surgical approach in patients undergoing appendectomy.

The main weaknesses of this study are its retrospective nature and the relatively small number of evaluated patients. We believe that larger and prospective studies should be conducted on this subject.

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