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Management of Antiplatelet Therapy Among Patients on Antiplatelet Therapy for Cerebrovascular or Peripheral Vascular Diseases Undergoing Elective Non-cardiac Surgery

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for 4 ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at Nicole.Floyd@va.gov.

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ABSTRACT

INTRODUCTION

The perioperative management of antiplatelet therapy (APT) for patients with cerebrovascular or peripheral vascular diseases remains unclear. This review was requested to assess the evidence for the following Key Questions:

1. Among patients on APT for cerebrovascular disease or peripheral vascular disease undergoing elective non-cardiac surgical procedures, including intraocular procedures, what are the benefits and harms of holding APT prior to surgery?

2. How does benefit/risk vary by the timing of discontinuation?

3. How does benefit/risk vary by type of surgical procedure, including intraocular procedures?

4. How does benefit/risk vary by type of APT?

5. How does benefit/risk vary by the timing of resuming APT?

METHODS

Data Sources and Searches

We conducted searches in PubMed from inception to 10/18/2016.

Study Selection

Studies were included if: (1) The patients underwent elective, non-cardiac surgery; (2) The majority of patients were on dual antiplatelet (DAPT) therapy or single PGY_{12} inhibitor (*eg*, clopidogrel) therapy; (3) The majority of patients were on APT for peripheral vascular stents or cerebrovascular stents; (4) Details regarding the pre- and perioperative management of APT were available; (5) The article present original data (*eg*,, not a review, commentary, or duplicate publication); (6) The article reported adverse events and/or bleeding outcomes; and (7) Published in the English language.

Data Synthesis and Analysis

Data extraction was completed in duplicate, and included: study design, setting (*eg*, academic, community, Veterans Affairs), number of sites, country of origin, sample size, operation(s), indication for APT, perioperative management including pre, peri and postoperative therapy (when available), and outcomes including major bleeding, thrombotic outcomes (*ie*, DVT, PE, Ischemic Stroke, MACE) and other major adverse events.

RESULTS

Results of Literature Search

Our literature searches and reference mining identified 613 potentially relevant citations, of which 56 abstracts were included and obtained as full-text publications. No study met all of our criteria. Thirteen publications provided some insight into the management of APT in patients with peripheral vascular (PVD) or cerebrovascular disease and are included in our final sample and grouped by procedure including: (1) specific (*ie,* the study only focused on one operation), (2) non-specific (*ie,* the study focused on several operations), (3) minor, including endoscopic procedures, and (4) intraocular procedures.

Summary of Results for Key Questions

Key Question 1

Thirteen observational studies provided some detail regarding the pre- and perioperative management of APT and its relationship to bleeding and thrombotic outcomes. Studies were generally small and indications were both inadequately described and deviated substantially from our target population. The perioperative management of APT agents was heterogeneous with significant contamination issues. Only 3 of the 13 studies showed an adverse association between APT agent and bleeding outcomes, primarily a function of intraoperative need for transfusion. There was no consistent difference in thrombotic, readmission, or mortality outcomes based on pre- and perioperative management of APT.

Key Question 2

Only a small subset of studies evaluated the timing of APT discontinuation with significant intra- and inter-study variation, limiting our ability to draw conclusions.

Key Question 3

Few studies reported results stratified by type of surgical procedure, and among those that did, there was no clear difference in outcomes depending on perioperative antiplatelet strategy.

Key Question 4

Studies were too small and did not include enough detail to associate outcomes with type of APT agent.

Key Question 5

Evidence for the impact of timing for resuming APT was absent from the identified literature.

DISCUSSION

Key Findings and Strength of Evidence

The overarching finding from this systematic review is that the available evidence regarding perioperative antiplatelet management in patients with cerebrovascular or peripheral vascular disease undergoing elective non-cardiac surgery is insufficient to conclusively guide clinical practice. The heterogeneity limited the ability to adequately assess the impact of APT

management. It is likely that factors other than the perioperative management of APT play a significant role in the differences in bleeding and thrombotic outcomes observed between studies. The strength (or quality) of the evidence was insufficient for all Key Questions.

Applicability

Only 2 studies were conducted in a Veterans Affairs setting, both from the same system reporting on the same procedure (endoscopy with polypectomy). Even though the remaining studies were not in VA populations, we judged these results as being moderately or even strongly applicable to VA since the enrolled patients were very likely to moderately or strongly resemble VA patients, except with respect to gender.

RESEARCH GAPS/FUTURE RESEARCH

There is obviously a large research gap, as we were unable to find evidence sufficient to reach conclusions for any of the key questions. The evidence does suggest that differences in outcomes due to perioperative antiplatelet management are likely to be smaller than differences in outcomes due to other clinical factors. This suggests that definitive answers to these questions are going to require clinical trials, and since the differences in outcomes are likely to be small, these studies will need to be large, on the order of many hundreds or even >1000 patients in each arm.

CONCLUSIONS

Published studies of the association between perioperative APT management and outcomes in patients with cerebrovascular or peripheral vascular disease undergoing elective non-cardiac surgery have challenging methodologic limitations and heterogeneous results, and do not provide sufficient evidence to moderately or strongly support any clinical recommendation. The results suggest that clinical factors other than perioperative APT management may be more responsible for bleeding and thrombotic outcomes. It is likely that a clinical trial of large size would be needed to more definitely provide evidence about these clinical decisions.

ABBREVIATIONS

ASA = aspirin
APT = antiplatelet therapy
DAPT = dual antiplatelet therapy
DVT = deep vein thrombosis
ESP = evidence synthesis program
IS = ischemic stroke
MACE = major adverse cardiac event
MI = myocardial infarction
PE = pulmonary embolus
PVD = peripheral vascular disease
SAPT = single antiplatelet therapy
TEP = technical expert panel
TIA = transient ischemic attack
VA = Veterans Affairs