



Management of Antiplatelet Therapy among Patients on Antiplatelet Therapy for Coronary or Cerebrovascular Disease or with Prior Percutaneous Cardiac Interventions Undergoing Elective Surgery: A Systematic Review

June 2017

Prepared for:

Department of Veterans Affairs
Veterans Health Administration
Quality Enhancement Research Initiative
Health Services Research & Development Service
Washington, DC 20420

Prepared by:

Evidence-based Synthesis Program (ESP) Center
West Los Angeles VA Medical Center
Los Angeles, CA
Paul G. Shekelle, MD, PhD, Director

Investigators:

Principal Investigator:

Paul Shekelle, MD, PhD

Co-Investigators:

Melinda Maggard Gibbons, MD, MSHS

Jesus G. Ulloa, MD, MBA

Ian T. Macqueen, MD

Christopher P. Childers, MD

Research Associates:

Isomi M. Miake-Lye, PhD

Roberta Shanman, MLS

Jessica M. Beroes, BS



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.

Recommended citation: Maggard Gibbons M, Ulloa JG, Macqueen I, Childers CP, Miake-Lye IM, Shanman R, Beroes JM, Shekelle PG. Management of Antiplatelet Therapy among Patients on Antiplatelet Therapy for Coronary or Cerebrovascular Disease or with Prior Percutaneous Cardiac Interventions Undergoing Elective Surgery: A Systematic Review. VA ESP Project #05-226; 2017.

This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the **West Los Angeles VA Medical Center, Los Angeles, CA**, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

ABSTRACT

INTRODUCTION

The perioperative management of antiplatelet therapy for patients with coronary stents remains unclear. This review was requested to assess the evidence for the following key questions:

1. Among patients on APT in conjunction with percutaneous coronary intervention (PCI) undergoing elective 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, Web of Science, and Scopus from inception of each database to 12/17/2015.

Study Selection

Studies were included if: 1.) The patients underwent elective, non-cardiac surgery, either entirely or in the great majority of reported cases; 2.) The patients were post-percutaneous coronary intervention with stent placement; 3.) The article presents original data (*eg*, not a review, commentary, or duplicate publication using the same data as another included publication); 4.) The article reports major adverse cardiac events (MACE) as a composite or any of the individual components (such as stent closure) or bleeding outcomes; 5.) The details of the preoperative and perioperative antiplatelet therapy were presented in sufficient detail to identify outcomes by management strategy; and 6.) The article was published in the English language. We did not exclude studies based on the type of APT management (*ie*, all P2Y12 agents were eligible).

Data Synthesis and Analysis

Data extraction was completed in duplicate. Data abstracted included the study design and data sources, details of the patient and the stent type, preoperative and perioperative antiplatelet therapy, type of surgery, outcomes, and statistical methods used.

RESULTS

Results of Literature Search

Our literature searches and reference mining identified 4,068 potentially relevant citations, of which 491 were included by at least one reviewer at the title screening stage. Of these, 100

abstracts were included and obtained as full-text publications. A total of 14 publications were identified that contributed as includes to our final sample.

Summary of Results for Key Questions

Key Question 1

Thirteen observational studies reported the details of preoperative APT, perioperative APT management, and outcomes, in sufficient detail to assess their association. The majority of studies were small, with less than 100 patients included, and the results were quite heterogeneous, with MACE rates and bleeding rates varying many-fold between studies reporting outcomes for the same combination of preoperative APT and perioperative management (such as preoperative dual antiplatelet therapy, holding both prior to surgery). In general, within studies the bleeding outcomes were reported at higher rates than the MACE outcomes.

Key Question 2

Evidence for the impact of timing of discontinuation of APT consists of very small case reports within larger studies, and demonstrated no identifiable trend. In one VA case control study, there was no association between stopping dual APT for at least 5 days versus some other strategy.

Key Question 3

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

Key Question 4

One large VA study did not find any evidence that the type of APT was associated with differences in MACE outcomes.

Key Question 5

Evidence for the impact of timing of resuming antiplatelet therapy 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 cardiac stents undergoing non-emergent surgery is insufficient to conclusively guide clinical practice. The heterogeneity observed limited the ability to adequately assess the impact of APT management for the wide range of procedures. It is likely that factors other than the perioperative management of APT play a role in differences in bleeding and MACE rates observed between studies. The strength (or quality) of the evidence was insufficient for all key questions.

Applicability

Several studies specifically assessed Veterans, including the largest study. 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 with cardiac stents were very likely to moderately or strongly resemble VA patients, except with respect to gender.

Research Gaps/Future Research

There is obviously a very 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, the trials must be very large, on the order of many hundreds or even >1000 patients in each arm of the trial.

Conclusions

Published studies of the association between perioperative APT management and outcomes in patients with coronary stents undergoing non-emergent surgery have challenging methodologic limitations and heterogeneous results, and do not provide sufficient evidence to moderately or strongly support any clinical recommendation. This heterogeneity, combined with small sample sizes, limits the ability to assess the impact of the different aspects of APT – timing of cessation, bridging, restarting therapy, and type of APT. Additionally, the varied range of invasiveness of the procedure, from skin excisions to major thoracic cases, contributes to the operative bleeding risk and MACE risk, yet many studies lacks sufficient detail to assess the impact of procedure on the outcomes. The results also suggest that clinical factors other than perioperative APT management may be in part responsible for MACE and bleeding outcomes. It is likely that a clinical trial of large size would be needed to more definitely provide evidence about this clinical decision.

ABBREVIATIONS TABLE

PCI = percutaneous coronary intervention

TEP = technical expert panel

MACE = major adverse cardiac events

APT = antiplatelet therapy

DAPT = dual antiplatelet therapy

SAPT = single antiplatelet therapy