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A Bridge Too Far? Risks and Benefits of Perioperative Bridging Therapy

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Abstract

➤ The long-term use of oral anticoagulants is common among high-risk patient populations for the prevention of thromboembolic events such as stroke, pulmonary embolism, etc. It is estimated that 15-20% of chronically anticoagulated patients will undergo a surgery or procedure that will require anticoagulation interruption annually. During this interruption period, “bridging” anticoagulant therapy is often utilized with unfractionated heparin or low-molecular weight heparin to ensure adequate anticoagulation is achieved. However, there has been an ongoing debate whether or not the benefits of perioperative anticoagulant bridging therapy outweigh its risks. This literature review focuses on whether or not forgoing anticoagulant bridging therapy increases the risk of peri/postoperative thromboembolic events. It also focuses on the whether or not initiating bridging therapy places patients at a higher risk for postoperative bleeding. Finally, it focusses on the current recommendations and whether or not utilization of individualized risk assessment tools increases efficacy and safety in regards to determining appropriate bridging therapy. The results of this literature review conclude that in low-risk patients there is sufficient evidence to support that non-bridging therapy is non-inferior to bridging therapy in the prevention of peri/postoperative thromboembolic events. There is also evidence to support that anticoagulant bridging therapy may place low-risk patients at a significantly higher risk for peri/postoperative bleeding events. Finally, there appears to be sufficient evidence to support the use of individualized risk assessment tools to help guide clinicians in their decisions regarding anticoagulant bridging therapy.

Introduction

- Oral anticoagulants are commonly used long-term in patients with atrial fibrillation, a history of a mechanical heart valve, or a recent history of thromboembolic events.
- It is estimated that 15-20% of chronically anticoagulated patients will undergo an elective or emergent surgery or procedure that will require anticoagulation interruption annually (Garwood et al., 2017).
- During this interruption period, “bridging” anticoagulant therapy is often utilized with unfractionated heparin or low-molecular weight heparin to ensure adequate anticoagulation is achieved and to reduce the risk of a thromboembolic event perioperatively (Ayoub et al., 2016).
- Current debate whether thromboembolic events caused by perioperative anticoagulant interruption posts a larger risk for patients than intra/postoperative bleeding for those who initiate bridging therapy (Douketis et al., 2015).

Statement of the Problem

- There is currently a lack of updated evidence-based guidelines and recommendations in regards to indications for perioperative bridging therapy.
- The most recent antithrombotic guidelines come from the American College of Chest Physicians (ACCP) in 2012.
- Current guidelines are a low-level recommendation (Level 2-C)
- To date, there remains to be an anticoagulant bridging therapy that is universally accepted which tailors an individual’s thromboembolic risk factors (Pengo et al., 2009).
- There is a need for additional high-level studies, and evidence-based guidelines to help guide clinicians.

Research Question

- Does forgoing perioperative anticoagulant bridging therapy in patients who are chronically anticoagulated place them at a higher risk for a postoperative thromboembolic event vs those patients who initiate bridging therapy?
- Does initiating perioperative anticoagulant bridging therapy in patients who are chronically anticoagulated place them at a higher risk for a major intra/postoperative bleeding event vs those patients who forgo bridging therapy?
- Should patients undergoing perioperative anticoagulant interruption be assessed using individualized risk assessment tools vs standardized bridging protocols to determine the need for anticoagulant bridging therapy?

Literature Review

Anticoagulant Bridging Therapy: Thromboembolic Risks

- Douketis et al. (2016) found from their BRIDGE trial that the placebo group was non-inferior when compared to the dalteparin group in reducing thromboembolic risk. Incidence rate of 0.4% (4 of 918) in placebo group compared to 0.3% (3 of 895) in the dalteparin group (risk difference, 0.1 percentage points, 95% confidence interval [CI], -0.6 to 0.8; P=0.01 for noninferiority).
- Bouillon et al. (2016) found no statistically significant difference in the occurrence of stroke/systemic embolism between the bridged and non-bridged groups at one-month of follow-up or later (HR 0.97, 95% CI 0.68 – 1.37, P=0.841 from 0-1 months follow-up, HR 0.98, 95% CI 0.67-1.43, P=0.899 from 2-3 months of follow-up).
- Ayoub et al. (2016) found no statistically significant difference in all-cause mortality (OR, 1.29; 95% CI, 0.15-11.52; P=0.82), cerebral vascular accident (OR, 0.93; 95% CI, 0.34-2.51; P=0.88), or thromboembolic events (OR, 0.72; 95% CI, 0.72-2.80; P=0.64) between the heparin bridging group and the non-bridging group at 30 days and up to 3 months.
- Ono et al. (2016) demonstrated similar incidences between the HBA and non-HBA groups for exogenous blood transfusion (23.3% vs 19.4%, P = 0.587) and thromboembolic events (4.1% vs 3.2%, P=0.755). The results demonstrate no significant rise in thromboembolic events with the non-HBA group as compared to the HBA group.

Anticoagulant Bridging Therapy: Bleeding Risks

- Douketis et al. (2016) found the occurrence of major bleeding events in the placebo group at 37 days post follow-up was 1.3% (12 of 918) compared to 3.2% (29 of 895) in the dalteparin group. These results indicate that the placebo group had superior outcomes in reducing bleeding risks as compared to the bridging group (relative risk, 0.41; 95% CI, 0.20 to 0.78; P=0.005 for superiority).
- Bouillon et al. (2016) as showed an increase in major bleeding events at one-month post-op follow-up in the bridging group as compared to the non-bridged group (0.47% vs 0.30%; P<0.001). However, in the 2-month and 3-month follow-ups there was no difference in bleeding events between the two groups (HR 0.93; 95% CI, 0.70-1.23, P=0.593).

- Siegal et al. (2012) found an increased risk in overall bleeding events was demonstrated in bridged patients compared to non-bridged patients (5.4 vs 3.6, 95% CI). Anticoagulant bridging therapy was associated with an overall increased risk of bleeding events in 13 studies (odds ratio, 5.40; 95% CI, 3.00-9.74) and major bleeding events in five studies (odds ratio, 3.60; 95% CI, 1.52-8.50).
- According to the Ayoub et al. (2016) meta-analysis there was a significantly reduced risk in postoperative bleeding identified in the non-bridging group as compared to the bridging group (OR, 0.41; 95% CI, 0.24-0.68; P=0.0006).
- Steinberg et al. (2015) found that the use of anticoagulant bridging therapy in patients with atrial fibrillation resulted in significantly higher overall bleeding risks (5.0% vs 1.3%; adjusted odds ratio, 3.84; P<0.0001).

Individualized Risk Assessments

- Palaniswamy and Selvaraj (2011) found that patients with atrial fibrillation who undergo perioperative interruption of oral anticoagulation should be stratified based on their risk of thromboembolic event compared to bleeding.
- Pengo et al. (2009) demonstrated that tailoring anticoagulant bridging therapy to a patient’s thromboembolic risk index was both an effective and safe strategy.
- Oprea, Noto, and Halaszynski (2016) performed a risk stratification review which stressed the importance of basing treatment with anticoagulant bridging therapy on patient-specific conditions.

TABLE 1
ACCP's suggested risk stratification for perioperative thromboembolism*

Risk category	Mechanical heart valve	Atrial fibrillation	Venous thromboembolism
High (>10%/yr risk of ATE or >10%/mo risk of VTE)	Any mechanical mitral valve Older aortic valve Recent (< 6 mo) stroke or TIA	CHADS ₂ score of 5 or 6 Recent (< 3 mo) stroke or TIA Rheumatic valvular heart disease	Recent (< 3 mo) VTE Severe thrombophilia
Moderate (4%-10%/yr risk of ATE or 4%-10%/mo risk of VTE)	Bileaflet aortic valve and one of the following: atrial fibrillation, prior stroke/TIA, hypertension, diabetes, heart failure, age > 75 yr	CHADS ₂ score of 3 or 4	VTE within past 3-12 mo Recurrent VTE Nonsevere thrombophilic conditions Active cancer
Low (<4%/yr risk of ATE or <2%/mo risk of VTE)	Bileaflet aortic valve without atrial fibrillation and no other risk factors for stroke	CHADS ₂ score of 0-2 (and no prior stroke or TIA)	Single VTE within past 12 mo and no other risk factors

Douketis et al. (2008). The perioperative management of antithrombotic therapy. CHEST, 133, 2995-3395, Copyright © 2008

CHADS₂ -> CHA₂DS₂VASc

CHADS ₂ Risk	Score	CHA ₂ DS ₂ VASc Risk	Score
CHF	1	CHF or LVEF ≤ 40%	1
Hypertension	1	Hypertension	1
Age > 75	1	Age ≥ 75	2
Diabetes	1	Diabetes	1
Stroke or TIA	2	Stroke/TIA/Thromboembolism	2
		Vascular Disease	1
		Age 65 - 74	1
		Female	1

Kirchoff et al. (2016). 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. European Heart Journal, 37(38), 2893-2962. Copyright © 2016

Discussion

- Current data does not support the use of routine bridging in low-risk anticoagulated patients.
- Multiple studies showed no statistically significant difference in the rates of thromboembolic events between the bridged and non-bridged groups.
- According to Siegel et al. “The risk of thromboembolic events was not significantly different in bridged and non-bridged patients”.
- Forgoing bridging was associated with a risk of bleeding that was significantly lower than the risk associated with bridging
- Douketis et al. (2016) found that “bridging conferred a risk of major bleeding that was nearly triple the risk associated with no bridging”
- Thromboembolic risk should be weighed against the bleeding risk associated with the procedure
- According to Siegel et al. (2012) patients receiving anticoagulant bridging perioperatively were at a 3-5-fold increase in overall and major bleeding events compared to patients who received no bridging therapy.
- Individualized risk assessment scores should be utilized when determining risk prior to administration of bridging therapy.

Applicability to Clinical Practice

- Forgoing bridging therapy may be non-inferior to bridging therapy in regards to thromboembolic prevention in low-risk patients.
- Bridging therapy is associated with a significantly higher risk of bleeding events compared to non-bridging therapy.
- Clinician's should utilize individualized risk assessment calculators (CHADS₂, HAS-BLED) to calculate a patients thromboembolic and bleeding risks to help guide clinicians in their decisions to use or forgo anticoagulant bridging therapy.

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