Bivalirudin as an anticoagulant for simultaneous integrated coronary artery revascularization – a novel approach to an inherent concern

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BACKGROUND: Simultaneous integrated coronary artery revascularization combines coronary artery bypass surgery and percutaneous coronary intervention into a single procedure. This approach provides immediate, complete and optimal myocardial revascularization in a less invasive manner. Because simultaneous integrated coronary revascularization necessitates two distinct anticoagulation protocols for the surgical and percutaneous aspects of the procedure, combining these anticoagulation protocols carries a bleeding risk. Using a single anticoagulant to facilitate the necessities of both aspects of the integrated approach may alleviate this risk.

CASE PRESENTATION: A 45-year-old man with an occluded left anterior descending artery and a moderately stenotic circumflex artery underwent simultaneous integrated coronary revascularization. Bivalirudin was used to achieve anticoagulation for the duration of the procedure. The patient was asymptomatic with excellent patency of both the bypass graft and the stented circumflex artery via angiography at 10 months.

CONCLUSION: Bivalirudin can be used to effectively achieve a unified anticoagulation protocol for simultaneous integrated revascularization.

Key Words: Angioplasty; Anticoagulants; Coronary disease; Revascularization; Stents; Surgery

Integrated coronary revascularization (ICR) combines the benefits of surgical coronary artery revascularization and catheter-based intervention. Specifically, ICR combines minimally invasive coronary artery bypass grafting (CABG) surgery of the left internal thoracic artery (LITA) to the left anterior descending artery (LAD), with percutaneous coronary intervention (PCI) of non-LAD flow, limiting lesions. This approach is an attractive option in patients with an occluded or complex LAD lesion and uncomplicated stenoses of other coronary arteries. Complete myocardial revascularization and the survival benefit of the LITA-to-LAD graft are both conferred in a much less invasive manner (1). At the London Health Sciences Centre, University Hospital (London, Ontario), ICR is performed simultaneously in a 'hybrid' operating room, with robotic-assisted CABG followed directly by PCI, avoiding delay between the two procedures.

Previous attempts at one-stage or simultaneous ICR have been limited by the increased risk of bleeding associated with combining two anticoagulation protocols (1). Heparin, with protamine reversal, remains

La bivalirudine comme anticoagulant en cas de revascularisation simultanée et intégrée des artères coronaires : Une nouvelle approche pour un problème inhérent

HISTORIQUE : La revascularisation simultanée et intégrée des artères coronaires combine le pontage aortocoronarien avec une intervention coronaire percutanée pour former une seule intervention. Cette approche assure une revascularisation myocardique immédiate, complète et optimale, de manière moins effractive. Ce type de revascularisation exige deux protocoles distincts d'anticoagulation pour les aspects chirurgical et percutané de l'intervention, mais leur association comporte un risque d'hémorragie. L'utilisation d'un seul anticoagulant afin de répondre aux deux aspects de l'approche intégrée pourrait soulager ce risque.

PRÉSENTATION DU CAS : Un homme de 45 ans présentant une occlusion de l'artère interventriculaire antérieure et une sténose modérée de l'artère circonflexe a subi une revascularisation simultanée et intégrée des artères coronaires. Il a reçu de la bivalirudine pour assurer l'anticoagulation pendant toute l'intervention. Le patient était asymptomatique et, à l'angiographie, il présentait une excellente perméabilité du pontage et de l'endoprothèse de l'artère circonflexe au bout de dix mois.

CONCLUSION : On peut utiliser la bivalirudine pour obtenir un protocole unifié d'anticoagulation en cas de revascularisation simultanée et intégrée.

the standard anticoagulant used in cardiac surgery, while PCI typically involves heparin, without reversal, combined with antiplatelet therapies such as clopidogrel and glycoprotein IIb/IIIa inhibitors. Clopidogrel, often considered to be the standard drug to use for preventing thrombosis during PCI, increases the risk of postoperative bleeding, the need for perioperative transfusion and the incidence of re-exploration when administered within four days of CABG (2). Glycoprotein IIb/IIIa inhibitors are also associated with an increased risk of hemorrhage and platelet transfusion when CABG is performed within several hours of PCI (3). However, without these antiplatelet therapies, PCI patients are at increased risk for acute stent thrombosis (1). The incompatibility of the anticoagulation protocols used for CABG and PCI are a major reason most institutions view ICR as a two-stage procedure, with CABG performed hours, days or weeks apart from PCI.

The present case report demonstrates the feasibility of using bivalirudin (The Medicines Company, USA) as a single anticoagulant for the duration of simultaneous ICR.

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Figure 1) Preoperative angiography demonstrating an occluded left anterior descending artery and a focal stenosis of the circumflex artery

CASE PRESENTATION

A 45-year-old ex-smoker with hyperlipidemia, hypertension and a strong family history of coronary artery disease presented with Canadian Cardiovascular Society class III angina. Other pertinent medical history included having sustained a myocardial infarction as well as undergoing PCI to the LAD eight months previously. Selective coronary angiography revealed a normal right coronary artery with collaterals to the LAD, an occluded LAD with retrograde filling and a focal stenosis of the circumflex artery (Figure 1).

The patient underwent simultaneous ICR, with robotic-assisted off-pump LITA-to-LAD CABG, followed by PCI of the circumflex artery using a drug-eluting stent (DES). The daVinci Surgical System (Intuitive Surgical, USA) was used to endoscopically harvest the LITA graft from the first to the sixth rib. After the pericardium was opened and the LAD identified, anticoagulation with bivalirudin (0.75 mg/kg bolus; 1.75 mg/kg/h infusion) was initiated. Anticoagulation was monitored by the activated clotting time. Once the time was greater than 300 s, the LITA was clipped and cut, and LITA-to-LAD anastomosis was performed manually through a nonrib-spreading incision. On completion of the surgical procedure, the operating room was converted into a fully functional cardiac catheterization suite with a digital C-arm. PCI with insertion of a DES to the circumflex artery was performed. After PCI, the bivalirudin infusion was continued for an additional 30 min while initiating antiplatelet therapy with 600 mg of clopidogrel via a nasogastric tube to achieve an overlap of the anticoagulation and antiplatelet regimes. Acetylsalicylic acid (81 mg) was then administered via a nasogastric tube 6 h postoperatively. Starting on postoperative day 1, the patient received once daily doses of 75 mg of clopidogrel and 81 mg of acetylsalicylic acid.

Intraoperative angiography revealed a widely patent LITA-to-LAD graft (Figure 2) and a widely patent stent in the circumflex artery (Figure 3). The patient experienced an uncomplicated convalescence and was discharged home on postoperative day 3. At a two-month follow-up examination, the patient reported no recurrent angina. Follow-up angiography performed at 10 months demonstrated a widely patent LITA-to-LAD graft with prompt antegrade and retrograde flow (Figure 4), and a normal circumflex artery with a widely patent stent (Figure 5). The patient remained in Canadian Cardiovascular Society class 0.

Figure 2) Intraoperative angiography demonstrating a widely patent left internal thoracic artery graft to the left anterior descending artery

Figure 3) Intraoperative angiography demonstrating a widely patent stent in the circumflex artery

DISCUSSION

With a 20-year patency rate of 90%, the LITA-to-LAD graft is the most reliable modality for LAD revascularization (4). A minimally invasive approach to this graft avoids the morbidity associated with both cardiopulmonary bypass and sternotomy (1). The addition of PCI provides complete revascularization while avoiding the invasiveness of a traditional CABG. Moreover, the demonstrated reduction in restenosis with DESs lends support to the use of PCI in non-LAD lesions. The single-stage approach described in the present report provides prompt verification of LITA-to-LAD graft patency and immediate complete revascularization. This alleviates any threat of myocardial infarction while awaiting a second procedure (1), as well as patient anxiety associated with two separate interventions.

Figure 4) Angiography demonstrating a widely patent left internal thoracic artery graft to the left anterior descending artery 10 months following simultaneous integrated coronary revascularization

Bivalirudin confers the benefits of simultaneous ICR without the bleeding risk associated with combining two anticoagulation protocols. Bivalirudin is a small, 20 amino acid synthetic peptide. It is a specific and reversible direct thrombin inhibitor that inactivates both clot-bound and fluid-phase thrombin, rapidly inducing anticoagulation and preventing platelet aggregation. It has a short half-life of 25 min and is predominantly eliminated through enzymatic degradation, decreasing renal involvement (5).

Bivalirudin is a safe and effective anticoagulant in patients with unstable angina undergoing PCI (5). Compared with heparin, bivalirudin is associated with fewer bleeding complications and reduced costs, and may provide protection against periprocedural ischemia (5). Although used less frequently in cardiac surgery, emerging evidence demonstrates bivalirudin to be a clinically feasible alternative to heparin during CABG. In patients undergoing on-pump CABG, bivalirudin and heparin have comparable rates of bleeding complications. Similar rates of perioperative blood loss using bivalirudin and heparin were also demonstrated in off-pump CABG. Moreover, it is suggested that graft flow may be superior in patients receiving bivalirudin. By inhibiting clot-bound thrombin and reducing endothelial proliferation, bivalirudin may protect newly sutured grafts. Furthermore, the effects of bivalirudin cannot be reversed because there is no antidote, allowing anticoagulation to persist during the early postoperative phase, preserving new grafts (5).

Figure 5) Angiography demonstrating a widely patent stent in the circumflex artery 10 months following simultaneous integrated coronary revascularization

The 45-year-old man described in the present report underwent successful robotic-assisted simultaneous ICR, utilizing bivalirudin-induced anticoagulation for the entire procedure, with excellent angiographic results, an uncomplicated convalescence and significant improvement of cardiac symptoms.

CONCLUSION

Bivalirudin has been demonstrated to be a feasible anticoagulant for simultaneous ICR, allowing for a minimally invasive approach to immediate, complete revascularization. Further investigation is necessary to thoroughly evaluate its clinical outcomes.

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