Revisão da terapia com heparinas nas síndromes coronarianas agudas

Reunião HCI Março 2012
José Fábio Fabris Júnior
Renato Sanchez Antonio
Sites of Anti-thrombotic Drug Action

Coagulation cascade

Intrinsic Pathway
Extrinsic Pathway

Plasma clotting cascade

Prothrombin

Factor Xa

AT III

Thrombin

Fibrinogen

Thrombolitics

Aspirin

ADP

Conformational activation of GPIIb/IIIa

Platelet aggregation

Platelet cascade

Platelet Agonists

Thromboxane A2

Prasugrel
Ticagrelor
Ticlopidine
Clopidogrel

GPIIb/IIIa inhibitors

Enoxaparin
DX-9065a

UF Heparin
Fondaparinux

Bivalirudin
Hirudin
Argatroban
Ximelagatran

Fibrin

Thrombus
Terapia Adjuvante
Impacto do Sangramento

Sangramento hospitalar em 34.146 pacientes com SCA (OASIS-1/2 +CURE)

Major bleeding (2.3%)

No Major bleeding

12.8%
P<0.0001

2.5%

0.0 5 10 15 20 25 30

Days

Mortality (%)

Note:
1. For PCI, wait at least 30 to 60 minutes after SC injection, depending on molecular weight of the agent (30 minutes for enoxaparin, 60 minutes for dalteparin).
2. Insufficient data are available to guide heparinization in patients who have received only 1 dose of SC LMWH.
3. Fewer data are available on patients treated with SC enoxaparin and no GP IIb/IIIa receptors antagonists undergoing PCI.
4. If the patient has been receiving dalteparin, switch to UFH, as there are no available data on transitioning from medical to interventional therapy when the last SC dose of dalteparin was given 8 to 12 hours before PCI.
5. Consideration can be given to enoxaparin 0.5 mg/kg in those patients not receiving concomitant GP IIb/IIIa receptor antagonist therapy.

Circulation 2011, 123:2022-2060; originally published online March 28, 2011
doi: 10.1161/CIRC0b013e31820f2f3e
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 75334
Copyright © 2011 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/123/18/2022

An erratum has been published regarding this article. Please see the attached page for:
http://circ.ahajournals.org/content/123/22/e525.full.pdf
http://circ.ahajournals.org/content/124/12/e337.full.pdf

Subscriptions: Information about subscribing to Circulation is online at
http://circ.ahajournals.org/subscriptions/
Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21201-2490. Phone: 410-528-4050. Fax: 410-528-8550. E-mail: journpermissions@lww.com
Reprints: Information about reprints can be found online at
http://www.lww.com/reprints

Downloaded from http://circ.ahajournals.org/ by guest on February 22, 2012
• As drogas devem ser denominadas anticoagulantes ao invés de antitrombínicos

• ALERTA INICIAL:

• A) Estratégia anticoagulante ideal?

• - Incertezas, equivalência de doses, duração da terapia, uso prévio de terapia anticoagulante (efeito residual)

• - Administração de regimes antiplaquetários distintos
• PREOCUPAÇÃO ADICIONAL
• - Os trabalhos baseiam-se no critério atual de não inferioridade (equivalência) entre as terapias ("margem de não inferioridade")
• - Dificuldade atual de trabalhos controlados por placebo
• - Recomenda-se cautela na avaliação dos resultados de não inferioridade
• Classe I: Estratégias anticoagulantes aceitáveis
• - a preferência por uma estratégia particular não é clara, devendo-se levar em consideração fatores tais como: erros de medicação, anticoagulação dupla, risco de sangramento, familiaridade local (particularmente se ATC planejada), necessidade de reversão do efeito anticoagulante
• Comitê redator desta diretriz julga, com base nos atuais estudos, ser difícil determinar a terapêutica anticoagulante ideal nos pacientes alocados para estratégia invasiva precoce
• Na estratégia não invasiva os resultados são menos confusos e apontariam em termos de preferência a utilização de foundaparinux, enoxaparina e HNF
• A bivalirudina não foi testada na estratégia não invasiva
• A duração de terapia anticoagulante permanece incerta


_Circulation_ 2011;124:e574-e651: originally published online November 7, 2011
doi: 10.1161/CIR.0b013e31823ba622
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 75231.
Copyright © 2011 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/124/23/e574

Subscriptions: Information about subscribing to Circulation is online at http://circ.ahajournals.org/subscriptions/
Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2435. Phone: 410-528-8550. E-mail: journalpermissions@lww.com
Reprints: Information about reprints can be found online at http://www.lww.com/reprints

Downloaded from http://circ.ahajournals.org/ by guest on February 22, 2012
Class IIb

1. In patients undergoing elective PCI with stent implantation treated with UFH and adequately pretreated with clopidogrel, it might be reasonable to administer a GP IIb/IIIa inhibitor (abciximab, or high-bolus epifibatide, or high-dose tirofiban), 419,625–626 (Level of Evidence: B)

See Online Data Supplement 24 for additional data regarding IV antiplatelet therapy.

In the era before DAPT, trials of adequately dose GP IIb/IIIa inhibitors in patients undergoing balloon angioplasty and coronary stent implantation demonstrated a reduction in the incidence of composite ischemic events with GP IIb/IIIa therapy as compared to heparin or aspirin alone. 413,415,618,620,621 Earlier RCTs of GP IIb/IIIa inhibitors were generally conducted in patients treated with UFH. In some trials, use of GP IIb/IIIa inhibitors is associated with some increased bleeding risk, and trials of these agents have generally excluded patients at high risk of bleeding (e.g., coagulopathy). 584,587–590,613–616,620–626 Thus, recommendations about use of GP IIb/IIIa inhibitors are best construed as applying to those patients not at high risk of bleeding complications. Abciximab, double-bolus epifibatide (180 mcg/kg bolus followed 10 minutes later by a second 180 mcg/kg bolus), and high-bolus dose tirofiban (25 mcg/kg) all result in a high degree of platelet inhibition, 425–426,429 and have been demonstrated to reduce ischemic complications in patients undergoing PCI, 426,606,607,613,615,618–621 and appear to lead to comparable angiographic and clinical outcomes. 426,621

Trials of GP IIb/IIIa inhibitors in the setting of STEMI and primary PCI were conducted in the era before routine stenting and shall not be described here. The results of these and more recent trials, as well as several meta-analyses, have yielded mixed results. 584–590 Therefore, it is reasonable to administer GP IIb/IIIa inhibitors in patients with STEMI undergoing PCI, although these agents cannot be definitively recommended as routine therapy. These agents might provide more benefit in selective use, such as in patients with large anterior MI and/or large thrombus burden. Trials of precatheaterization laboratory (e.g., ambulance or emergency room) administered GP IIb/IIIa inhibitors in patients with STEMI undergoing PCI with or without fibrinolytic therapy, have generally shown no clinical benefit, and GP IIb/IIIa inhibitor use in this setting may be associated with an increased risk of bleeding. 505–506,612 Studies of intracoronary GP IIb/IIIa inhibitor administration (predominantly using abciximab) consist of several small RCTs, retrospective analyses, retrospective and prospective registries, cohort analyses, and case reports. Although most of these published studies have reported some benefit of intracoronary administration in terms of angiographic parameters, infarct size, left ventricle myocardial salvage, and composite clinical endpoints, several other studies have not detected any benefit with intracoronary administration. 286,287–290

Trials of GP IIb/IIIa inhibitors in patients with UA/NSTEMI undergoing PCI demonstrated reduced ischemic outcomes, particularly in those with high-risk features such as positive biomarkers. Most trials were conducted in a prior PCI era and without P2Y12 inhibitor pretreatment, although several trials have also demonstrated benefit in patients with high-risk features pretreated with clopidogrel. 414,618,619 In most studies of stable patients undergoing balloon angioplasty or coronary stenting, treatment with GP IIb/IIIa inhibitors resulted in a reduction of composite ischemic events, primarily enzymatically defined MI. 413–418,618,620,619,634,635 More contemporary trials of patients pretreated with a thienopyridine have not demonstrated any benefit with GP IIb/IIIa inhibitor therapy in patients with stable symptoms undergoing elective PCI. 418,625–626

5.7.4. Anticoagulant Therapy

5.7.4.1. Use of Parenteral Anticoagulants During PCI: Recommendation

Class I

1. An anticoagulant should be administered to patients undergoing PCI (Level of Evidence: C)

Anticoagulant therapy prevents thrombus formation at the site of arterial injury, on the coronary guidewire, and in the catheter used for PCI. 5 With rare exceptions, 428 all PCI strokes occur as a form of anticoagulant therapy. It is the consensus of the writing committee that PCI should be performed with the use of some form of anticoagulant therapy. Suggested dosing regimens of parenteral agents used in PCI are given in Table 12. Recommendations for antiplatelet and anti-thrombin pharmacotherapy in PCI are given in Table 13.

5.7.4.2. UFH: Recommendation

Class I

1. Administration of IV UFH is useful in patients undergoing PCI (Level of Evidence: C)

As the only anticoagulant available for PCI for many years, UFH became the standard of care by default. 8 The dose of UFH for PCI has been based on empiricism and experience from RCTs. Suggested UFH dosing regimens are given in Table 12. When UFH is used during PCI, most cardiologists assess the degree of anticoagulation by measuring the activated clotting time. Although measurements are useful to show that an anti-IIa anticoagulant has been given, the value of the activated clotting time in current practice has been questioned. Although studies in the balloon angioplasty era did demonstrate a relationship between activated clotting time levels and ischemic complications, 423–425 more recent analyses from the coronary stent era have not found a clear relationship between activated clotting time and outcomes. 348,623–637 There may, however, be a modest relation between bleeding and activated clotting time levels. 348,637 In addition, not only are there differences between activated clotting time levels measured by Hemocon and HemoTec devices, but also these levels have less than optimal precision. 348 Thus, although traditional target activated clotting time levels are included in this document, the utility of measured activated clotting time levels in current practice should be considered uncertain.
Table 12. Dosing of Parenteral Anticoagulants During PCI

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patient Has Received Prior Anticoagulant Therapy</th>
<th>Patient Has Not Received Prior Anticoagulant Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>UFH</td>
<td>• IV GPI planned: additional UFH as needed (eg, 2000 to 5000 U) to achieve an ACT of 300 to 250 s &lt;br&gt;• No IV GPI planned: additional UFH as needed (eg, 2000 to 5000 U) to achieve an ACT of 250 to 300 s for HemoTec, 300 to 350 s for Hemochron</td>
<td>• IV GPI planned: 50 to 70 U/kg bolus to achieve an ACT of 200 to 250 s &lt;br&gt;• No IV GPI planned: 70 to 100 U/kg bolus to achieve target ACT of 250 to 300 s for HemoTec, 300 to 350 s for Hemochron</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>For prior treatment with enoxaparin, if the last SC dose was administered 8 to 12 h earlier or if only 1 SC dose of enoxaparin had been administered, an IV dose of 0.3 mg/kg of enoxaparin should be given. &lt;br&gt;• If the last SC dose was administered within the prior 8 h, no additional enoxaparin should be given.</td>
<td>0.5 to 0.75 mg/kg IV bolus</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>For patients who have received UFH, 30 min, then give 0.75 mg/kg IV bolus, then 1.75 mg/kg per h IV infusion</td>
<td>0.75 mg/kg bolus, 1.75 mg/kg per h IV infusion</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>For prior treatment with fondaparinux, administer additional IV treatment with an anticoagulant possessing anti-Xa activity, taking into account whether GPI receptor antagonists have been administered.</td>
<td>N/A</td>
</tr>
<tr>
<td>Argatroban</td>
<td>200 mcg/kg IV bolus, then 15 mcg/kg per min IV infusion</td>
<td>350 mcg/kg bolus, then 25 mcg/kg per min IV infusion</td>
</tr>
</tbody>
</table>

ACT indicates activated clotting time; IV, intravenous; GPI, glycoprotein inhibitor; N/A, not applicable; PCI, percutaneous coronary intervention; SC, subcutaneous; and UFH, unfractionated heparin.

Most cardiologists remove femoral sheaths when the activated clotting time falls to <150 to 180 seconds or when the activated partial thromboplastin time falls to <50 seconds. Full-dose anticoagulation is no longer used after successful PCI procedures. Almost all large clinical trials have enrolled patients who underwent transfemoral PCI, but recent small studies assessing the transradial approach have used similar doses of UFH and similar activated clotting time target levels.

5.7.4.3. Enoxaparin: Recommendations

Class I
1. An additional dose of 0.3 mg/kg IV enoxaparin should be administered at the time of PCI to patients who have received fewer than 2 therapeutic subcutaneous doses (eg, 1 mg/kg) or received the last subcutaneous enoxaparin dose 8 to 12 hours before PCI.444,445 (Level of Evidence: B)

Class Ib
1. Performance of PCI with enoxaparin may be reasonable in patients either treated with “upstream” subcutaneous enoxaparin for UA/NSTEMI or who have not received prior antithrombin therapy and are administered IV enoxaparin at the time of PCI.446-448 (Level of Evidence: B)

Class III: HARM
1. UFH should not be given to patients already receiving therapeutic subcutaneous enoxaparin.449,450 (Level of Evidence: B)

Trials of enoxaparin relevant to PCI include both studies in which patients with UA/NSTEMI were started on upstream subcutaneous enoxaparin therapy that was continued up to the time of PCI and trials in which patients who had received no prior antithrombin therapy were treated with IV enoxaparin at the time of PCI.444-445,446-447 In the SYNERGY (Superior Yield of the New strategy of Enoxaparin, Revascularization and Glycoprotein IIIb/IIIa Inhibitors) trial, there was an increased incidence of bleeding in those treated with upstream enoxaparin, later attributed at least in part to the fact that some patients being treated with enoxaparin were also administered UFH at the time of PCI (so-called “stacking”).448-449 Almost all patients undergoing elective PCI who are administered enoxaparin (0.5 mg/kg IV) will have a peak anti-Xa level >0.5 IU/mL.447 Most clinical studies have used a regimen of 0.5 to 0.75 mg IV.447 Several studies have used this regimen in elective patients and those with STEMI.448 Patients who have received multiple doses of subcutaneously administered enoxaparin who undergo PCI within 8 hours of the last subcutaneous dose generally have adequate degrees of anticoagulation to undergo PCI, but the degree of anticoagulation may diminish in the 8- to 12-hour period after the last subcutaneous dose. In such patients, as well as in patients who have received only 1 subcutaneous dose of enoxaparin, the addition of enoxaparin (0.3 mg/kg IV) at the time of PCI provides an additional degree of anticoagulation and has become standard practice.448-449,450,451 Patients who undergo PCI >12 hours after the last subcutaneous dose are usually treated with full-dose de novo anticoagulation using an established regimen (eg, full-dose UFH or bivalirudin).

5.7.4.4. Bivalirudin and Argatroban: Recommendations

Class I
1. For patients undergoing PCI, bivalirudin is useful as an anticoagulant with or without prior treatment with UFH.425,426 (Level of Evidence: B)

Downloaded from http://circ.ahajournals.org/ by guest on February 22, 2012
Table 13. Recommendations for Antiplatelet and Antithrombin Pharmacotherapy at the Time of PCI

<table>
<thead>
<tr>
<th>ORAL ANTIPLATELET AGENTS</th>
<th>COR</th>
<th>LOE</th>
<th>REFERENCES</th>
<th>RELEVANT CAUTIONS/COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>I</td>
<td>B</td>
<td>501-364,560-563</td>
<td>N/A</td>
</tr>
<tr>
<td>P2Y12 inhibitors</td>
<td>I</td>
<td>A</td>
<td>564-566</td>
<td>A loading dose of a P2Y12 inhibitor should be given to patients undergoing PCI with sterile.</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>I</td>
<td>B</td>
<td>564-566</td>
<td>900 mg loading dose now recommended.</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>I</td>
<td>B</td>
<td>567</td>
<td>Contraindicated in patients with prior TIA/CVA: Class III: Harm; LOE B.</td>
</tr>
<tr>
<td>Ticagrelir</td>
<td>I</td>
<td>B</td>
<td>566</td>
<td>Generally not recommended in patients &gt;75 y of age (Section 5.7.2).</td>
</tr>
<tr>
<td>GP IIb/IIIa inhibitors (abciximab, double-bolus epifibatide, High-bolus dose tirofiban)</td>
<td></td>
<td></td>
<td></td>
<td>Issues of patient compliance may be especially important.</td>
</tr>
<tr>
<td>No clopidogrel pretreatment</td>
<td>STEMI Ib</td>
<td>A</td>
<td>564-550</td>
<td></td>
</tr>
<tr>
<td>UAH/STEMI I</td>
<td>A</td>
<td>613-618</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHD: Ib</td>
<td>B</td>
<td>619-621</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel pretreatment</td>
<td>STEMI Ib</td>
<td>C</td>
<td>564-550</td>
<td>UAH/STEMI I: Ib</td>
</tr>
<tr>
<td>UAH/STEMI I: Ib</td>
<td>B</td>
<td>619,622-624</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANTI-XA INHIBITORS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UFH</td>
<td>I</td>
<td>C</td>
<td>623,627-645</td>
<td></td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>I</td>
<td>B</td>
<td>623,627-645</td>
<td>Lower bleeding rates associated with bivalirudin are mitigated when used concomitantly with a GPI.</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>IIb</td>
<td>B</td>
<td>646-650</td>
<td>Donor based on whether or not GPI was administered.</td>
</tr>
<tr>
<td>Anti-Xa inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>II Harm</td>
<td>C</td>
<td>651,652</td>
<td></td>
</tr>
</tbody>
</table>

ACT indicates activated clotting time; COR, class of recommendation; CVA, cerebrovascular accident; FDA, US Food and Drug Administration; GP, glycoprotein; GPI, glycoprotein IIb/IIIa inhibitor; IC, intracoronary; IV, intravenous; LOE, level of evidence; MI, myocardial infarction; N/A, not applicable; PCI, percutaneous coronary intervention; SC, subcutaneous; SHD, stable ischemic heart disease; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack; UAH/STEMI, unstable angina/non-ST-elevation myocardial infarction; and UFH, unfractionated heparin.

2. For patients with heparin-induced thrombocytopenia, it is recommended that bivalirudin or argatroban be used to replace UFH.634.640 (Level of Evidence: II)

Bivalirudin is being increasingly used in clinical practice670 as evidence emerges from clinical trials across the spectrum of CAD.638-442 In individual trials and meta-analyses, the use of bivalirudin has been associated with reduced bleeding compared with UFH plus a GP IIb/IIIa inhibitor, although concerns about ischemic events have emerged in individual studies.639,647-645 Longer-term follow-up of the major bivalirudin trials, however, suggests that small or nominal increases in ischemic events have not translated into long-term consequences and that treatment at or before the time of PCI with bivalirudin may mitigate any increased early ischemic risk.643,644 Thus, a treatment strategy of bivalirudin compared with heparin (or enoxaparin) plus GP IIb/IIIa inhibitor appears to lower the risk of bleeding complications. The lower bleeding rates associated with bivalirudin (compared with UFH plus a GP IIb/IIIa inhibitor) are mitigated when used concomitantly with a GP IIb/IIIa inhibitor.639 A strategy of use of provisional GP IIb/IIIa inhibitor in patients treated with bivalirudin is widely accepted.634,640,646

In patients with heparin-induced thrombocytopenia,671-672 a direct-thrombin inhibitor (argatroban) has been approved as an alternative parenteral anticoagulant to be used during PCI.642 The use of bivalirudin for heparin-induced thrombocytopenia has been reported as well.640

5.7.4.5. Fondaparinux: Recommendation

Class III: HARM

1. Fondaparinux should not be used as the sole anticoagulant to support PCI. An additional anticoagulant

Downloaded from http://circ.ahajournals.org by guest on February 22, 2012
with anti-IIa activity should be administered because of the risk of catheter thrombosis.\textsuperscript{433,435} \textbf{(Level of Evidence: C)}

Fondaparinux, a pentasaccharide, is an indirect factor Xa inhibitor but has no effect on thrombin. On the basis of reports of catheter thrombosis when fondaparinux is used alone during primary PCI,\textsuperscript{431,435} the writing committee recommends that an anticoagulant with anti-IIa activity be used in patients undergoing PCI.\textsuperscript{431,432} One study reported that clinical outcomes were better when fondaparinux was replaced during PCI by a standard dose of UFH (85 U/kg, 60 U/kg with GP IIb/IIIa inhibitors) rather than by a low dose (50 U/kg).\textsuperscript{675}

5.7.5. No-Reflow Pharmacological Therapies: Recommendation

Class IIa

1. Administration of an intracoronary vasodilator (adenosine, calcium channel blocker, or nitroprusside) is reasonable to treat PCI-related no-reflow that occurs during primary or elective PCI.\textsuperscript{674-689} \textbf{(Level of Evidence: B)}

See Online Data Supplement 25 for additional data regarding no-reflow therapies.

No-reflow is a broad term used to describe 2 distinct entities. The first is "interventional no-reflow" attributed to vessel dissection or downstream embolization of grafts, dislodged during PCI, usually in the setting of atherectomy, thrombus, or degenerated SVGs. The second entity is suboptimal reperfusion of an infarct artery, attributed to endothelial injury in addition to embolization and vasospasm. Angiographic no-reflow is the most obvious sequela of the same pathophysiology that produces abnormal TIMI frame counts and TIMI blush scores, so these measures are often used interchangeably. The principal clinical sequela of no-reflow is myocardectomy. Efforts to prevent no-reflow overlap with strategies to reduce MI size and prevent periprocedural MI.

For interventional no-reflow, several therapies have proven effective after no-reflow has started. These include adenosine, calcium channel blockers, and nitroprusside.\textsuperscript{574,670,671} \textbf{(Level of Evidence: B)}

5.8. PCI in Specific Anatomic Situations

5.8.1. CTOs: Recommendation

Class IIa

1. PCI of a CTO in patients with appropriate clinical indications and suitable anatomy is reasonable when performed by operators with appropriate expertise.\textsuperscript{699-711} \textbf{(Level of Evidence: B)}

See Online Data Supplements 26 to 28 for additional data regarding CTOs.

Approximately one third of patients with suspected CAD who undergo coronary angiography have \textgreek{z} 1 CTO (defined as occlusion of a duration \textgreater 3 months).\textsuperscript{704} Although stress-induced ischemia can be elicited in the majority of patients with CTO despite the presence of collaterals,\textsuperscript{702,703} only 8% to 15% of these patients undergo PCI.\textsuperscript{704,705} The disparity between the frequency of CTOs and percutaneous treatment underscores not only the technical and procedural complexities of this lesion subtype but also the clinical uncertainties regarding which patients benefit from CTO revascularization. Studies suggest that patients who undergo successful, rather than failed, recanalization of CTOs fare better in terms of symptom status and need for CABG, as well as LV function.\textsuperscript{710} However, the impact of successful CTO recanalization on long-term survival remains unsettled.\textsuperscript{711,712} The decision to try PCI for a CTO (versus continued medical therapy or surgical revascularization) requires an individualized risk-benefit analysis encompassing clinical, angiographic, and technical considerations. Consultation with a cardiothoracic surgeon and use of the Heart Team approach in cases of CTO in which a large territory is subtended and/or multivessel CAD is present are frequently done.

From a technical perspective, successful recanalization of CTOs has steadily increased over the years because of adoption of dedicated wires, novel techniques, and increased operator experience.\textsuperscript{702} In patients who undergo successful CTO recanalization, use of DES significantly reduces the need for repeated target-vessel revascularization, compared with BMS and balloon angioplasty, without compromising safety.\textsuperscript{703,713-716}

5.8.2. SVGs: Recommendations

Class IIb

1. EPIs should be used during SVG PCI when technically feasible.\textsuperscript{553-555} \textbf{(Level of Evidence: B)}

Class III: NO BENEFIT

1. Platelet GP IIb/IIIa inhibitors are not beneficial as adjunctive therapy during SVG PCI.\textsuperscript{712,717,720,721} \textbf{(Level of Evidence: B)}

Class III: HARM

1. PCI is not recommended for chronic SVG occlusions.\textsuperscript{722-724} \textbf{(Level of Evidence: C)}