Work in progress report - Coronary
Different anticoagulation strategies in off-pump coronary artery bypass operations: a European survey

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Abstract

In order to determine anticoagulation strategies in OPCAB a questionnaire survey among 750 European cardio-thoracic surgeons was performed. Questions addressed volume of OPCAB procedures performed, intra- and perioperative heparinization and antiplatelet therapy, as well as perioperative management. A total of 325 (43.7%) questionnaires were returned and validated. Perioperative protocols for administration of antiplatelets differed among the respondent surgeons. Perioperative prophylaxis of thrombosis (low or high molecular weight heparin) is performed by 78%. Intraoperative heparin dosage range between 70 U/kg to 500 U/kg. 60% of respondents prefer a low-dose regimen (<150 U/kg). Correspondingly, the lowest activated clotting time (ACT) during surgery is accepted to be 200 s by 24%, 250 s by 18% and 300 s by 26% of surgeons. Protamine is used by 91% of respondents, while 52% perform a 1:1 reversal. A cell-saver and antifibrinolytics are used by 70% and 40%, respectively. Interestingly, 56% of respondents think bleeding in OPCAB patients is not reduced when compared to on-pump CABG. In addition, 34% of respondents believe there is an increased risk of early graft occlusion following OPCAB. This survey demonstrates widely different intra- and perioperative anticoagulation strategies for OPCAB procedures among European surgeons.

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Keywords: OPCAB; Anticoagulation

1. Introduction

Off-pump coronary artery bypass (OPCAB) has progressively been accepted as a standard technique in many centers. However, in contrary to on-pump coronary artery bypass grafting (CABG), coagulation patterns during this type of procedure remain poorly investigated. Only a limited number of studies focus on hemostatic changes during OPCAB [1, 2]. Some authors described a reduction in postoperative blood loss following OPCAB and proposed alternate patterns of activated coagulation-fibrinolysis as compared to on-pump procedures [3]. Conversely, concerns have been raised regarding a possible OPCAB-associated procoagulant activity, and consequently a higher risk of perioperative venous thrombosis and early graft occlusion. There is thus a need to clarify these aspects. However, since uniform perioperative anticoagulation standards in OPCAB procedures are lacking we performed a questionnaire survey in order to determine current practice.

2. Material and methods

The questionnaire consisting of 15 questions, some divided into sub-questions (Table 1) was sent out via regular mail to 750 European cardio-thoracic surgeons whose addresses were generated according to an internet search (e.g. using the homepage of the European Society of Cardio-Thoracic Surgeons). It was not known whether the surgeon practiced OPCAB or not. Anonymous response was intended. Questionnaires were sent in the following 16 countries: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. In order to increase the response rate the questionnaire was sent out twice. The second questionnaire was accompanied by a letter in order to avoid double response. All responses were tabulated and analyzed.

3. Results

The response rate was 328/750 (43.7%). Response rates according to countries are listed in Table 2. Three surgeons responded that they did not perform off-pump technique. The remaining 325 returned questionnaires were valid for resulting. Out of cumulative possible answers (counted as one answer per question), only a very few were not interpretable, reflecting a high completeness (>99.7%) of responded questionnaires.

3.1. Question no. 1

The approximate number of isolated CABGs performed per year in the respondent’s institution varied between 30 and 3500 (median 500).
Table 1
The questionnaire

<table>
<thead>
<tr>
<th>Question</th>
<th>Response rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1 How many isolated CABG procedures (no concomitant surgery) are performed in your center per year?</td>
<td></td>
</tr>
<tr>
<td>No. 2 How many OPCAB procedures are performed in your center per year?</td>
<td></td>
</tr>
<tr>
<td>No. 3 Is the number of OPCAB procedures increasing/decreasing/stable in your hospital?</td>
<td></td>
</tr>
<tr>
<td>No. 4 Do you administer antiplatelets (aspirin and/or plavix) before OPCAB? – if yes: which drug?</td>
<td></td>
</tr>
<tr>
<td>No. 5 Do you administer antiplatelets (aspirin and/or plavix) after OPCAB? – if yes: which drug?</td>
<td></td>
</tr>
<tr>
<td>No. 6 Do you administer thrombosis prophylaxis with heparin? – if yes: starting before/after surgery?</td>
<td></td>
</tr>
<tr>
<td>No. 7 Have you noticed a higher incidence of deep vein thrombosis (DVT) or pulmonary embolism (PE) after OPCAB?</td>
<td></td>
</tr>
<tr>
<td>No. 8 How much heparin do you administer during OPCAB?</td>
<td></td>
</tr>
<tr>
<td>No. 9 Which ACT do you consider as lower limit during OPCAB?</td>
<td></td>
</tr>
<tr>
<td>No. 10 Do you reverse heparin with protamine? – if yes: full dose reversed/half dose reversed/other protocol</td>
<td></td>
</tr>
<tr>
<td>No. 11 Do you think that partial heparinization determines a lower incidence of perioperative bleeding?</td>
<td></td>
</tr>
<tr>
<td>No. 12 Do you use a cell-saving device during OPCAB?</td>
<td></td>
</tr>
<tr>
<td>No. 13 Do you use antifibrinolytics during OPCAB? (yes (routinely)/no/yes (with specific indication)) – if yes: which drug?</td>
<td></td>
</tr>
<tr>
<td>No. 14 Is your average postoperative bleeding less in OPCAB than in CABG with CPB?</td>
<td></td>
</tr>
<tr>
<td>No. 15 In your opinion: is there an increased risk of early graft occlusion in OPCAB? – if yes, possible reasons: technical problems/procoagulant disorders/others</td>
<td></td>
</tr>
</tbody>
</table>

Table 2
Survey response rate

<table>
<thead>
<tr>
<th>Country</th>
<th>No. mailed</th>
<th>Responded</th>
<th>Response rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>15</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Belgium</td>
<td>51</td>
<td>18</td>
<td>35</td>
</tr>
<tr>
<td>Denmark</td>
<td>22</td>
<td>9</td>
<td>41</td>
</tr>
<tr>
<td>Finland</td>
<td>19</td>
<td>13</td>
<td>68</td>
</tr>
<tr>
<td>France</td>
<td>105</td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td>Germany</td>
<td>195</td>
<td>93</td>
<td>48</td>
</tr>
<tr>
<td>Greece</td>
<td>17</td>
<td>5</td>
<td>29</td>
</tr>
<tr>
<td>Italy</td>
<td>78</td>
<td>28</td>
<td>36</td>
</tr>
<tr>
<td>Netherlands</td>
<td>26</td>
<td>13</td>
<td>50</td>
</tr>
<tr>
<td>Norway</td>
<td>7</td>
<td>5</td>
<td>71</td>
</tr>
<tr>
<td>Portugal</td>
<td>11</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Spain</td>
<td>45</td>
<td>17</td>
<td>38</td>
</tr>
<tr>
<td>Sweden</td>
<td>19</td>
<td>9</td>
<td>47</td>
</tr>
<tr>
<td>Switzerland</td>
<td>23</td>
<td>19</td>
<td>83</td>
</tr>
<tr>
<td>Turkey</td>
<td>16</td>
<td>8</td>
<td>50</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>101</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>750</td>
<td>328</td>
<td>43.7</td>
</tr>
</tbody>
</table>

3.2. Question no. 2

Per year, a mean of 120±131 OPCAB procedures were performed per center (median 78, min. 0, max. 800). This represents 24.6±24.1% (median 16%) of the total volume of isolated CABGs performed.

3.3. Question no. 3

Among responding surgeons, 38% reported an increase of OPCAB procedures in their centers as compared to the previous years. Conversely, 37% reported stable numbers of OPCAB cases, whereas 23% reported a decreasing trend. The answer was either not given or not interpretable in 2%.

3.4. Questions no. 4 and 5

Perioperative protocols for administration of antiplatelets differed significantly among surgeons (see Fig. 1a).

3.5. Question no. 6

Perioperative prophylaxis of thrombosis with heparin (not specifying dosage and differentiation between high- and low-molecular-weight heparin) is practiced by 78% (n=258) of respondents (Table 3). Out of these, 29% (n=74) start heparin prophylaxis before surgery, whereas the majority (67%, n=173) start it after the operation. The remaining 11 returned questionnaires (4%) did not specify the use of heparin.

3.6. Question no. 7

The vast majority of responding surgeons (97%) did not notice a higher incidence of deep venous thrombosis or pulmonary embolism in OPCAB.

3.7. Question no. 8

Heparin dosage is highly variable and ranges between 70 U/kg and 500 U/kg. Nevertheless, 60% of surgeons prescribe low-dose regimens (<150 U/kg) and 18% use a dose of 200 U/kg (see Fig. 1b).

3.8. Question no. 9

Correspondingly, the accepted lower limit of activated clotting time (ACT) also largely differs between the respondents. Nevertheless, most of them tolerate a lower ACT value between 200 and 250 s (Fig. 1c).

3.9. Question no. 10

Only very few respondents (9%) do not intend to reverse heparin at the end of surgery whereas 91% use protamine. However, the protocol for reversal differs between the institutions with a full dose reversal (1:1) being performed by 52% of respondents and a half dose scheme being preferred by 30%. Other reduced dose protocols (such as a two-third dose) are chosen by 10% (Fig. 1d).
Fig. 1. Percentage of answers to question 4 and 5 (a), question 8 (b), question 9 (c), and question 10 (d). (NA, not applicable; ACT, activated clotting time).

Table 3
Survey response: results of 325 questionnaires.

<table>
<thead>
<tr>
<th>Q. no.</th>
<th>Question</th>
<th>Yes (%)</th>
<th>No (%)</th>
<th>NI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q. 6</td>
<td>Thrombosis prophylaxis with heparin?</td>
<td>78</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Q. 12</td>
<td>Cell-saving device used?</td>
<td>70</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Q. 13</td>
<td>Use of antifibrinolytics?</td>
<td>40</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>Q. 14</td>
<td>Average bleeding less in OPCAB?</td>
<td>42</td>
<td>56</td>
<td>2</td>
</tr>
<tr>
<td>Q. 15</td>
<td>Increased risk of early graft occlusion?</td>
<td>34</td>
<td>63</td>
<td>3</td>
</tr>
</tbody>
</table>

Data are given in percent of total answers. (Q., Question; DVT, deep vein thrombosis; PE, pulmonary embolism; NI, not interpretable answer).

3.10. Question no. 11

Approximately two-thirds of responding surgeons (63%) do not think that partial heparinization determines a lower incidence of perioperative bleeding.

3.11. Questions no. 12 and 13

The use of a cell-saver device or the administration of antifibrinolytics in order to reduce perioperative blood loss is often used (Table 3). In total, 40% of respondents (n=129) use antifibrinolytics during OPCAB, from whom 55% (n=71) only in the presence of specific indications such as redo-surgery or in patients with preoperative combined antplatelet therapy. Aprotinin is exclusively chosen by 57% of the respondents using antifibrinolytics whereas lysinanalogue are preferred by 16%, and 6% use either aprotinin or lysinanalogue. Surprisingly, 21% of respondents using antifibrinolytics do not answer which type they used.

3.12. Question no. 14

Average bleeding is thought by 182 respondents (56%) to be not reduced in OPCAB patients as compared to patients operated with a conventional approach (Table 3).

3.13. Question no. 15

One hundred and eleven respondents (34%) think that OPCAB technique is a risk factor for early graft occlusion. Among them, 80% invoke technical problems as the major reason. Interestingly, 33% of respondents think that a procoagulant disorder associated with the OPCAB technique may increase the risk of early graft occlusion. Other reasons were brought by 10% of responding surgeons.
4. Discussion

Perioperative anticoagulation strategies as well as peri-procedural and long-term antiplatelet therapy are critical in CABG patients. Standard protocols have clearly been defined for cardiac operations performed with CPB. Conversely, no strategy has clearly been identified for OPCAB procedures so far. Indeed, we are able to confirm the lack of standardized protocols in OPCAB surgery in this European survey: inhomogeneous practice regarding anticoagulation protocols, antiplatelet therapy and the use of antifibrinolytics. The lack of guidelines and the subsequent various protocols may thus not only impede the quality of the results associated with OPCAB procedures, but also question the interpretation of OPCAB results when reports are compared to each other or to standard on-pump operations.

Over the last few years, OPCAB procedures became very popular among certain cardiac surgeons. This approach remains, however, severely criticized by others who question the safety of the procedure and the quality of the results [4, 5]. In fact, the concomitant development of surgical techniques, extracorporeal technologies and the improvement of perioperative management have dramatically reduced the risks associated to standard cardiac operations performed on-pump. Therefore, following an initial boost in OPCAB surgery, several centers have now limited or even stopped their off-pump cardiac surgical activities whereas others on the contrary have increased it. Our current observation confirms this phenomenon as 23% of respondents reported a trend toward a decrease of OPCAB procedures in their center, whereas 38% reported an increasing tendency. The percentage of OPCAB procedures as compared to the total number of isolated coronary revascularization is also largely different between the centers. Interestingly, only very few surgeons reported that they stopped their OPCAB activity. However, it must be hypothesized that a significant number of the non-responding surgeons did not answer the questionnaire because they do not perform OPCAB or they stopped this activity. In order to define this aspect, we should perhaps have proposed a question asking more specifically if they have performed OPCAB procedures in the past or if they have no experience with this approach.

Unlike in conventional on-pump CABG, only a very limited number of studies focus on hemostatic changes during OPCAB [1, 2]. In the current observation, perioperative anticoagulation strategies appeared to differ widely among our respondents. Nevertheless, there seems to be a trend toward a lower dose heparinization as compared to standard dosage administered in on-pump CABG. Indeed, 60% of respondents administer at the beginning of their OPCAB procedure 150 U/kg heparin or a lower dose whereas only 16% use a similar dose as for on-pump CABG. Correspondingly, 68% of the respondents accept a perioperative ACT value of 300 or lower. Studies specifically analyzing various heparinization protocols in OPCAB operations, and their influence on laboratory markers and/or clinical outcomes, have not been reported yet. We demonstrated in accordance to others [1], that activation of coagulation and fibrinolysis is reduced in OPCAB patients as compared with on-pump CABGs, even if a very low-dose heparin protocol (70–100 U/kg) was used [3]. However, full heparinization may nevertheless offer a better protection from intravascular coagulation, especially in patients with heparin resistant thrombin activity.

Because of the absence of a CPB system, intra-operative cell salvage strategies employing a cell-saver are used by 70% of the responding surgeons. Even though the utilization of a cell-saver device in OPCAB surgery has been recently shown to improve the postoperative hemoglobin concentrations and slightly reduce the transfusion requirements [6]. However, adverse effects of this approach such as hemolysis and activation of the inflammation cascade were also reported.

The use of antifibrinolytics was also questioned in our survey. Interestingly, it appeared that a reduced number of surgeons administer antifibrinolytics in OPCAB procedures as compared to on-pump operated patients. Indeed, even though some studies underlined the effectiveness of both aprotinin [7] or lysinanalogues [8] in OPCAB procedures, only 40% of our responding surgeons mentioned their routine administration. Out of them, 55% report using antifibrinolytics only in specific indications, such as redo-surgery or in patients under combined antiplatelet therapy.

At the end of an OPCAB procedure, reversal of heparin with protamine is performed by the majority (91%) of responding surgeons. One-half (52%) use complete reversal (1:1 ratio), whereas the remaining surgeons perform half-dose reversal (38%), two-third dose reversal or other protocols. According to recent literature, a reduced-dose reversal might not increase the risk of postoperative bleeding [9]. Comparing full-dose heparin reversal vs. half-dose reversal or no reversal, the investigators showed a reduced postoperative bleeding in the heparin reversal groups, but demonstrated also the absence of significant difference between the full-dose and the lower-dose groups. In addition, another study demonstrated the normalization of ACT levels in the majority of OPCAB patients reversed with a half-dose protamine, even when a full heparinization protocol was used [10].

The current practice of peri-operative antiplatelet therapy also differed widely between the responding surgeons. Similarly as for on-pump CABG procedures, the early use of aspirin is adopted for OPCAB patients by the majority of respondents. However, there seems to be a trend towards the administration of aspirin already before surgery. This attitude may be justified as the platelet dysfunction caused by CPB is obviously absent in OPCAB patients. Only very few surgeons administer clopidogrel before an OPCAB procedure. In fact, clopidogrel exposure prior to on-pump CABG is well known to increase the risk of postoperative bleeding, the need for perioperative transfusion and the incidence of re-exploration. Conversely, clopidogrel following on-pump CABGs is superior to aspirin [11]. In addition, recent data demonstrate that early postoperative administration of clopidogrel is safe after OPCAB [12]. In our current study, 15% of respondents administer clopidorel after OPCAB (alone or combined with aspirin).

Standard prophylaxis of thrombosis in the perioperative period is reported by the majority (78%) of responding surgeons. However, as opposed to other non-cardiac surgical procedures, two-thirds start the prophylactic measure...
with heparin postoperatively (as it seems to be standard scheme in elective on-pump CABG in many centers), whereas one-third administer heparin in a prophylactic dosage already prior to surgery. The overwhelming majority (97%) of respondents did not notice a higher incidence of deep venous thrombosis or pulmonary embolism in OPCAB compared to on-pump CABG. This is in accordance with a recently published study in which the rate of venous thrombosis and pulmonary embolism was low in both OPCAB and on-pump CABG patients [13].

In conclusion, our current study highlights the lack of consensus regarding peri-operative anticoagulation management in OPCAB patients. Indeed, the various attitudes observed among more than 300 European cardiac surgeons definitely demonstrate the need for systematic studies in this field. Our findings are in accordance with other investigators, who demonstrate also widely different anticoagulation regimens in OPCAB patients in North American [14] and Northern European [15] centers.

Acknowledgments

Many thanks to all the responding participants in this survey.

References


eComment: HIT in OPCAB surgery

Authors: [Karsten Knobloch, Plastic, Hand and Reconstructive Surgery, Hannover Medical School, Hannover 30625, Germany; Andreas Gohritz, Marcus Spies, Peter M. Vogt
doi:10.1510/icvts.2007.169086A
Given the fact that 78% of the respondent surgeons use low or high molecular weight heparin for perioperative prophylaxis of thrombosis, potential adverse effects of heparin should be considered [1].

As such, thrombocytopenia is a common problem in cardiovascular patients, and heparin-induced thrombocytopenia (HIT) is therefore frequently suspected following cardiac surgery. Currently, it is not clear whether OPCAB surgery is associated with the same or a different incidence of HIT I or HIT II in contrast to on-pump cardiac surgery.

It has been suggested that both functional (platelet activation tests) and immunologic assays (antigen assays) are necessary in every patient to establish the diagnosis of HIT. Screening with thromboelastography has been proposed recently [2]. The prevalence of heparin/platelet factor 4 antibodies is currently under investigation. As far as cardiac surgery is concerned, the high prevalence of antibodies to the heparin/PA4 complex after cardiac surgery and the low rate of thromboembolic complications in this population suggest that the antibody alone does not confer an increased risk of thrombotic complications [3]. This is supported by a recent retrospective analysis [4]. The authors concluded that postoperative platelet count fall between days 5 and 10 increases diagnostic specificity for HIT, irrespective of whether this platelet count fall occurs after postoperative platelet count recovery or is superimposed upon persisting postoperative thrombocytopenia.

A recent survey among 487 cardiac surgery patients with postoperative thrombocytopenia (50% drop in platelet count or absolute count <100,000/µl) at least one enzyme-linked immunosorbent assay for HIT platelet factor 4 antibodies was performed [5]. Postoperative infections occurred more frequently in HIT+ patients, including sepsis and pneumonia. The HIT+ patients also had a higher rate of renal failure requiring hemodialysis and acute limb ischemia. Thirty-day mortality was significantly higher in the HIT+ group (24.8% vs. 15.2%, P = 0.019). Postoperative HIT emerged as an independent predictor of renal failure (OR = 1.73, P < 0.001) and thromboembolic complications (OR = 2.39, P = 0.02). In conclusion, greater awareness of the potential devastating sequelae may allow earlier detection of HIT in OPCAB as well as in on-pump cardiac surgery.

References


eComment: Is anticoagulation management more significant for patients undergoing off-pump bypass than for those after CABG?

Authors: Efstratios Apostolakis, Department of Cardiothoracic Surgery, University Hospital of Patras, 22500 Rion Patras, Greece; Ioanna Koniari doi:10.1510/icvts.2007.169086B

Actually, this survey confirms that there is a great variation as far as the strategy for OPCAB operations is concerned between several Cardiothoracic Departments [1]. As a result, the observed inhomogeneous practice regarding anticoagulation protocols, antiplatelet therapy, use of antifibrinolytics and the further lack of guidelines for OPCAB reflects the difficulty of even multi-center trials to lead to reliable conclusions [2]. Besides, the fact that a cell-server being a miniature of CPB – is used by 70% of surgeons may explain the report by several studies of comparable results between CABG and OPCAB concerning the incidence of stroke, SIRS, neuro-cognitive disorders, haemorrhage etc. [3]. The fact that 34% of surgeons consider OPCAB as an independent risk factor for the early occlusion of grafts [1], indicates that this surgical method has not yet been proved reliable. Also, it would be interesting to inform us which was the surgical experience (operations/year) of these surgeons. Moreover, the fact that two-thirds (67%) of surgeons support the postoperative administration of antiplatelet agents in combination with low-dose heparine reflects their fear of complications, not only of DVT – whose risk is relatively lower [4], but also the early thrombosis of anastomoses or grafts.

In our opinion, anticoagulation therapy plays a more significant role for the patients undergoing OPCAB compared with CABG, where there is a notable decreased coagulation ‘status’ (decreased platelets levels, hemodilution, consumption of coagulation factors, fibrinolysis, preoperative administration of antiplatelet agents and heparine, etc.) [5]. Consequently, the creation of guidelines concerning the optimal perioperative strategy during OPCAB remains an important aim to improve the early and late results.

References