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Question	**Response**
Two Sentence Summary for Table of Contents In the first concise sentence please state the study design and the most important finding of this manuscript. In the second sentence state the most important conclusion. If accepted for publication, this summary will appear on the table of contents under the title of your article. **Examples** Intercostal artery reimplantation did not	Late open conversions after EVAR by using exclusively infrarenal clamping of the endograft in this single center retrospective study had a low renal morbidity rate (7.7%). This technique is feasible, safe and effective. It allows simplifying the surgical technique, and may avoid renal and visceral complications related to a suprarenalclamping.

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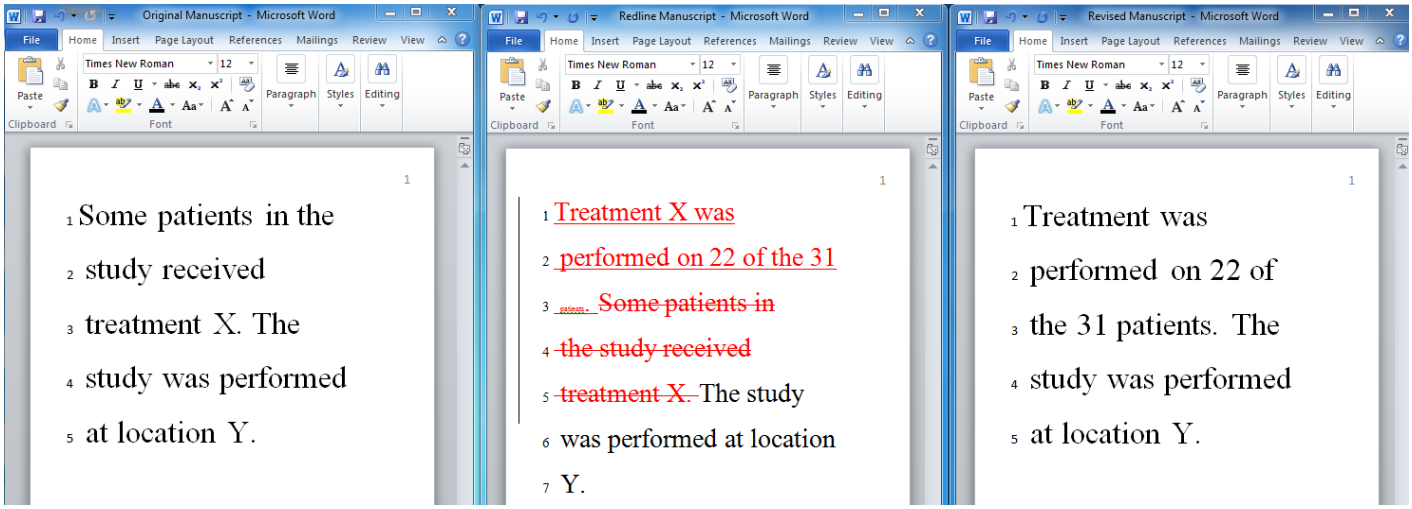

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Manuscript Title: Infrarenal endograft clamping in late open conversions after endovascular abdominal aneurysm repair

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Example: Reviewer #1
1. How many patients received treatment X?
Response: We have clarified that 22 patients received treatment XYZ.
"Treatment X was performed on 22 of the 31 patients." Redline page 1 lines 1-2.

<PASTE REVIEWER COMMENTS HERE TO BEGIN>

Reviewer #1:
Introduction
1. Page 3 line 16. Omit "Nowadays"

We erased "nowadays", as suggested by the reviewer.
Redline P4 L8 "*EVAR is currently the primary mode of treatment for abdominal aortic aneurysms (AAA) […]*"

Materials and Methods
1. * Page 5 lines 10-12. Why was complete graft explant needed for type II endoleaks (4/27) 14.8%? Why not open the sac and over sew the leak(s)? Was this not feasible?

Actually, 3 out of 4 type II endoleaks were multiple (associated with a type I or III endoleak); see redline P8 L19-21 "In 3 cases (11.1%) multiple types of endoleak were

present (2 cases of type I associated with type II, and 1 case of type II associated with a type III)". Finally, only one "pure" type II endoleak was treated with open conversion. In this case, sacculotomy and lumbar/inferior mesenteric artery ligation was not feasible since the right limb of the endograft displaced during clamping manoeuvres. Thus, we performed an open conversion with proximal preservation of the endograft (which was caught by the clamp).
In case of "pure" type II endoleaks our first approach is an endovascular embolization. If unsuccessful, we typically perform an attempt to repair the endoleak without graft removal (as stated in the materials and methods section "Patients who underwent open surgical attempts to repair endoleaks without graft removal (i.e. sacculotomy and lumbar artery ligation) were excluded", redline P5 L6-8).

To clarify, we added to the text "Indications for LOC were *[…], or if surgical attempts to repair the endoleak without graft removal was not technically feasible*" in the materials and methods section, according to the Reviewer's comment (see redline P5 L26, P6 L1).

Results
1. * Page 7 line 13. None of your cases were done for infection. Since infection requires complete removal of graft material and some of your patients had partial removal was infection an exclusion criteria? If so would state in methods. If not would state this and say if infection was suspected the intention was complete removal. Did any cases you did end up requiring supraceliac or suprarenal clamping after you exposed the infrarenal aorta with the intent to clamp there, and if so were they excluded?

None of our cases were done for infection since we did not experience such complication during our study period. We agree with the reviewer that in this case a complete removal of the endograft is mandatory, as we already stated in the discussion section (Redline P14 L13 "In this case, a complete explantation of the endoprosthesis is mandatory").
In our series, the abdominal aorta was always clamped in an infrarenal position, with no need of temporary suprarenal clamp positioning, as stated in both the results section (redline P9 L5-6 "Technical success rate was 100%: an infrarenal cross-clamping was possible in all cases, with no need of temporary suprarenal clamp positioning") and the discussion section (redline P12 L14-15 "In our series, the abdominal aorta was always clamped in an infrarenal position, regardless of the presence and the characteristics of the proximal part of the endograft"), as demonstrated by the technical success of 100%.
In the results section, we changed "No endograft infection underwent LOC in our series" to "*We did not experience cases of endograft infection […] in our series*" to clarify the text according to the Reviewer's suggestions (Redline P8 L22-23).

Discussion
1. *Pages 10-11 lines 12-14. You need to mention that in your series a length of neck suitable for clamping was required. Can you look back in your series and figure out the range and mean neck length? How does this copare to other series' that used supra-celiac and/or suprarenal clamping?

In literature, the choice to perform an infrarenal rather than a suprarenal clamping is not based on the length of the neck, but on the characteristics of the endograft (primarily the presence of a suprarenal bare stent) and/or the operator's preference. Furthermore, these data (neck length) are not reported in literature. We can look back in our series and figure out the range and mean neck length, but, for the reasons stated above, a comparison with the literature is impossible. Can the Editor advise, please?

The low feasibility of this technique in case of juxta- or para-renal aneurysm is already discussed in the limitation paragraph (redline P14 L4-13 "A potential limitation of this technique may be related to its lack of applicability in cases of complete aneurysmal degeneration of the proximal aortic neck with subsequent development of a juxta-renal, para-renal or thoraco-abdominal aneurysm"). Anyhow, according to the Reviewer's suggestion, we added this information in both the "materials and methods" and "results" section:
Materials and Methods - Redline P6 L10-12 "*Exclusion criteria for this technique were the presence of endograft infection or complete aneurysmal degeneration of the proximal neck with consequential transformation in juxta-renal or thoraco-abodominal aneurysm*."
Results - Redline P8 L22-23 "*We did not experience cases of endograft infection nor complete degeneration of the proximal neck in our series*"

2. *Page 13 line 18. Need a limitations paragraph.

The limitations of the study have already been discussed in a dedicated paragraph (see Redline P14 L4-13 "Despite the potential limitations of a retrospective analysis […]. A potential limitation of this technique […]. Finally, we did not experience stent-graft infections [...]").
Can the Editor advise, please?

3. Page 14 line 5. Would include "in properly selected patients" after "method".

The text has been modified accordingly (Redline P15 L8-9 "This method, *in properly selected patients*, allows to simplify the surgical technique, and potentially avoids renal and visceral complications that may be related to a suprarenal or supraceliac clamping.").

Reviewer #2:
*1) Were these consecutive or selected LOC patients? Have any LOC patients in your practice required supra-renal or supra-celiac clamping? Have you treated patients with distal graft migration due to neck enlargement that needed more complex open repair or fenestrated/branched EVAR?

These were consecutive LOC patients, with no need of supra-renal clamping, not even temporary (cf. answer to the Reviewer #1, section "Results" n.1: "*In our series, the abdominal aorta was always clamped in an infrarenal position, with no need of temporary suprarenal clamp positioning, as stated in both the results section (redline P9*

L5-6) and the discussion section (redline P12 L14-15), as demonstrated by the technical success of 100%.").

No, we have not treated patients with distal graft migration due to neck enlargement that needed more complex OR or FEVAR. The low feasibility of this technique in case of juxta- or para-renal aneurysm is discussed in the limitation paragraph (redline P14 L10-11: "[…] *we recommend endovascular therapy using a fenestrated or branched endograft[…]*").
According also to Reviewer #1's suggestion (please see answer to question n.1, discussion section, Reviewer #1), we modified the text in both the "materials and methods" and "results" section to make it clearer:
Materials and Methods - Redline P6 L10-12 "*Exclusion criteria for this technique were […] complete aneurysmal degeneration of the proximal neck with consequential transformation in juxta-renal or thoraco-abodominal aneurysm*."
Results - Redline P8 L22-23 "*We did not experience cases of […]complete degeneration of the proximal neck in our series*"

*2) You mention that all patients underwent post-operative surveillance ultrasounds at 1 month, 3 months, 6 months and then annually, but you fail to report the results of these studies. Please include data regarding these studies. If they were all unremarkable, do you still require them?

This is the standard follow-up protocol of our centre after open repair, to assess the patency of the graft, the status of the anastomosis and patient's long-term survival.
Long term survival rates has already been calculated by Kaplan-Meier curves and included in the text (please see Redline P10 L14-16 and Figure 5 "The survival rate was estimated at 84% at 6 months, 78% at 5 years and 58% at the 10-year follow-up by means of the Kaplan-Meier method (Fig. 5). No aneurysm-related death occurred during follow-up").
Data about the patency of the graft and the status of the anastomosis have been added, according to the Reviewer's suggestion: "*Aortic grafts remained patent during the follow-up, and no anastomotic stenosis nor aneurysm degeneration were recorded*." (Redline P10 L12-13).

*3) With your technique of preserving and sewing to the proximal endovascular graft remnant, you could unclamp and discover a residual type I endoleak. Did this occur in your series, and if it did, how did you manage it?

We did not sew to the proximal endovascular remnant, but we sew together the Dacron graft, the aortic wall AND the proximal endovascular remnant, as described in the materials and methods section (see Redline P6 L6-9 "the proximal covered stent was used as a "neo-neck", sewing together the Dacron graft, the aortic wall and the endograft (Fig. 2 and 3) in order to minimize the risk of late dilatation of the residual infrarenal aorta and to avoid further complications due to a late migration of the remaining stentgraft"). In all cases the stitches were passed as deeply as possible as far as the juxtarenal aorta and through the covered stent mimicking endobanding (cf. Bonvini et al., reference number 11, who utilized a similar technique for the proximal anastomosis, but with a suprarenal clamping). Thus, a residual type Ia endoleak is

virtually impossible to occur.

*4) Additional data on operative blood loss, need for transfusions, operative time, etc. might be helpful. What were the factors that led to multi-system organ failure in your two elective LOC deaths?

We added data on operative blood loss, need for transfusions and operative time. The text has been modified accordingly.

Redline P5 L11-13 "*[...]and surgical data ([...], operative time, blood loss and need for transfusions) were obtained for analysis*"

Redline P9 L14-16 "*Mean operative time was 239 ± 80 min. Median estimated blood loss was 1000 mL (range: 500 – 3500 mL). Median transfused red blood cells units during surgery were 0.5 (range: 0 – 6 units)*"

Concerning elective LOC deaths, the 2 cases of MOF condition likely resulted from pulmonary infection secondary to prolonged ventilation. We added this information in the text (Redline P9 L18-20): "These two patients died of MOF during ICU stay*, which likely resulted from pulmonary infection secondary to prolonged ventilation*".

*5) I find table IV confusing. It would be clearer if you included columns with the data for surviving patients and patients without renal morbidity as well as for those who died or suffered renal morbidity. Since there were only two deaths and two cases of renal morbidity, however, it is probably best to delete this table and simply state that there were no statistically significant pre-operative predictors of mortality and that only aneurysm rupture predicted post-operative renal dysfunction. Also, I am not clear as to why for renal dysfunction the denominator is 26 and not 28.

As suggested by the Reviewer, we erased Table IV, and we simply stated that there were no statistically significant preoperative predictors of mortality, and that only aneurysm rupture predicted postoperative renal dysfunction (Redline P9 L20-21 "No predictive risk factor of early mortality was found", P10 L5-6 "*Only aneurysm rupture predicted postoperative renal dysfunction*", P10 L7-8 "~~These data are summarized in Table IV~~").

The denominator for renal dysfunction is 26 because, for early morbidity analysis, we excluded postoperative deaths, as we already stated in the original version of the manuscript (see Redline P9 L22 "Early mordibity rate was calculated by excluding postoperative deaths (n=26)"). Since these patients died for MOF (and therefore developed every possible complication, including respiratory, intestinal, renal, sepsis, …) the statistical analysis would have been biased.

Minor Points:
1) Introduction, page 4, line 7: "evaluating"

We corrected this typo (Redline P4 L21-23 “The aim of this study is to assess the

feasibility of an infrarenal aortic cross-clamping during LOC after EVAR, by *evaluating* the technical aspects and outcomes in our single centre experience”).

2) Methods and Materials, page 5, line 10: "symptomatic"
The text has been modified accordingly (Redline P5 L23-24 “Indications for LOC were the presence of a type I or III endoleak, or other types of endoleaks when *symptomatic*”).

3) Results, page 7, lines 6-10: better would be: "In 27 patients the indication for LOC was persistent endoleak: 20 type I, 4 type II associated with sac enlargement, 3 type III, and 3 type IV (endotension defined as sac enlargement in the absence of identifiable endoleak)."

The text has been modified as suggested by the Reviewer.

Redline P8 L13-19 “*In 27 patients the indication for LOC was persistent endoleak: 20 type I, 4 type II associated with sac enlargement, 3 type III, and 3 endotensions (defined as sac enlargement in the absence of identifiable endoleak).*” “~~In 27 patients, indication for LOC was represented by the presence of an endoleak, specifically: 20 patients presented a type I endoleak, 4 patients a type II associated with aneurysm growth, 3 patients a type III endoleak and 3 patients a type IV / endotension (this group was defined as an aneurysm sac enlargement without the evidence of an endoleak on the preoperative CT-scan and intraoperatively).~~”

4) Page 8, lines 2-3: "Resection of the stent graft was always performed at the level of the fabric to minimize the risk of erosion." I am not sure what this means. Risk of erosion of what? Please explain this in more detail.

Resection of the stent-graft was always done at the level of the fabric to reduce the risk that the cut stent struts would eventually damage the new graft or the suture line. We explained this concept in more detail in the text, as suggested by the Reviewer: “*In case of partial removal, resection of the endoprosthesis was always performed at the level of the fabric to minimize the risk that a cut metal stent would finally erode the new graft or the suture line*”. (Redline P9 L9-11)

5) Discussion, page 11, line 2: "…or even impossible due to the presence of the suprarenal free-flow." What does this mean? What is "suprarenal aortic free-flow"?

We revised this sentence to make it clearer: “*In addition, in case of a well incorporated endoprosthesis with suprarenal fixation, cannulation of the renal arteries for protection by cristalloid perfusion may be difficult or even impossible to perform due to the presence of the bare metal stent at the level of the target arteries*”.

Redline P12 L10-13

6) Page 11, lines 10-14: The explanation is obvious. Your numbers are so small that statistical comparison of your mortality rates with the mortality rates seen in other series is meaningless. Please rewrite this section.

We rewrote this section, as suggested by the Reviewer: "~~*Currently, we are not able to explain this* difference.~~ *However, this discrepancy may be related to the small number of urgent patients in our series*".

Redline P12 L24-26

7) Page 11, line 15: "One of the major complications of LOC is aortic or renal dissection or occlusion that may occur……"

We revised the text as suggested by the Reviewer.

Redline P13 L1-2 "One of the major complication of LOC is ~~represented by~~ aortic or renal dissection *or occlusion* that may occur [...]"

8) Page 13, line 4-7: "…..may be related to its lack of applicability in cases of aneurysmal degeneration of the aortic neck with subsequent development of a juxtarenal, pararenal, or thoracoabdominal aneurysm. In this case, we recommend endovascular ….."

The text has been modified according to the Reviewer's suggestion.

Redline P14 L6-10 "*A potential limitation of this technique may be related to its lack of applicability in cases of complete aneurysmal degeneration of the proximal aortic neck with subsequent development of a juxta-renal, para-renal or thoraco-abdominal aneurysm. In this case, we recommend endovascular [...]*"

9) Figure V: Please include standard errors as isobars or numerically at time intervals up to 102 months.

A modified image has been provided.

Reviewer #3:
1. Page 5, lines 16-17-How did you cut the stents and were you capable of totally arresting blood flow in those patients in whom you had to clamp across and transect the proximal stent graft?

We did not cut the stents in our series, the endograft was cut at the level of the fabric (please see answer to Reviewer #2, Minor point n.4). The blood flow is arrested completely without experiencing particular issues, even in case of endograft clamping.

Figure 2 is quite explicative for both points, since it shows where the endograft is cut, and that the clamping is effective.

2. Page 6, lines 18-21- What percentage of your total EVAR volume underwent LOC? It would be of value to know whether your conversion rate is consistent with the 3.7% you quoted from the literature given the large number of LOCs that you have performed. It would be a good percentage to be able to quote if you data is consistent with previous reports.

The percentage is 4.6% (28/607). However, we decided not to report this value, since a portion of the LOC we performed did not undergo initial EVAR in our centre (i.e. 3 patients). And, at the same time, we assumed that a portion of our EVAR underwent LOC in other centres. Finally, we thought that a percentage calculated on these data may not correspond to reality. Can the Editor advise, please?

3. Page 7, lines 8-9- a type 4 endoleak is not endotension. Endotension is a type 5 endoleak. This should be corrected along with table 2

We agree with the Reviewer. In the first version of this article, we decided to group together type IV and type V endoleaks, since sometimes they may be difficult to discriminate. We analyzed again our databases, and we allocated these 3 cases in the endotension group (finally, we had no case of type IV endoleak).The text and the table have been modified accordingly.

Redline P2 L15 ("[...]3 ~~type IV /~~ endotensions[...]"), P8 L13-19 ("[...]and 3 ~~type IV /~~ endotensions (defined as sac enlargement in the absence of identifiable endoleak)[...]")

4. *Page 7, lines 21-23- Please describe the technique you utilized to remove a suprarenally fixated stent graft (75%) in its entirety, with an infrarenal cross clamp, or was that never performed? Were those cases always managed with partial stent graft preservation?

A suprarenal fixated endograft was removed in its entirety only if it was not caught by the infrarenal clamp (e.g. in case of a distal migration of the endoprosthesis). Cases where the proximal endograft was clamped were managed with partial preservation, as described in the materials and methods section (Redline P6 L6-9 "[...]the proximal covered stent was used as a "neo-neck", sewing together the Dacron graft, the aortic wall and the endograft [...]").

To clarify, we added an example in the text: "The proximal stents were completely removed in case the main body of the endograft was not caught by the aortic clamp *(e.g. in case of distal migration of the endograft, Fig. 1)*" (Redline P6 L5-6).

5. *Page 8, lines 11-22- I feel the operative blood loss (excluding the ruptures) should be included in the morbidity analysis as this may be a reason to consider total versus partial graft excision in LOC

Data about the operative blood loss were added as suggested by the Reviewer (cf. answer n.4, Reviewer #2). It was not a risk factor for early mortality (cf. Redline P9 L20

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Abstract and key words

Objective. The aim of this study is to report the technical aspects and outcomes of late open conversions (LOC) after endovascular aneurysm repair (EVAR) in a single centre, by using exclusively infrarenal clamping of the endograft as an alternative to suprarenal or supraceliac aortic clamping.

Materials and Methods. A retrospective analysis of EVAR requiring late explants (>30 days) from January 1996 to October 2016 was performed. Patients' demographics, type of endograft, duration of implant, reason for removal, extent of stent-graft removal, type of reconstruction, 30-day mortality, postoperative complications and log-term survival were obtained for analysis.

Results. During the study period, 28 patients required LOC. The mean age at conversion was 75.11 years ± 6.65; 26/28 (92.86%) were male. Grafts were excised after a median of 41.4 months (range, 5.97 – 112.67 months), with 21/28 explants (75%) performed electively. Multiple types of EVAR devices have been explanted: suprarenal fixation was present in the 75% of the cases. Indication for LOC was the presence of an endoleak in 27 cases (20 type I, 4 type II associated with aneurysm growth, 3 type III, 3 ~~type IV /~~endotensions; in 3 cases multiple types of endoleak were present) and graft thrombosis in 1 case. All patients underwent transperitoneal approach with infrarenal clamping. No patient required revascularization of visceral or renal vessels. Complete removal of the stentgraft was performed in 8/28 cases, partial removal in the remaining 20 cases (with conservation of the proximal portion in 16/20 cases). Technical success was 100%. Overall 30-day mortality was 7.14% (2/28). Thirty-day mortality was 9.5% in elective patients, and 0% in urgent setting; this difference was not statistically significant (p=.56). Postoperative kidney injury rate was 7.7% (2/26). Mean follow-up was 47.37 months ± 55.67 SD (range, 0.23 – 175.07 months). The estimated 5-year survival rate was 78%. No aneurysm-related death nor additional procedure occurred during follow-up.

Conclusions. LOC after EVAR using the infrarenal clamping of the endograft is a feasible and effective technique, with satisfactory post-operative mortality and morbidity. This method allows

simplifying the surgical technique, and may avoid renal and visceral complications related to a suprarenal or supraceliac clamping.

Key words: abdominal aortic aneurysm, open surgical conversion, endovascular repair, EVAR, late complications

Text

Introduction

Since the initial description by Parodi in 1991(1), endovascular aneurysm repair (EVAR) has gained widespread acceptance. In the current vascular practice, the selection of endovascular surgery for aneurysm repair is based upon both the assessment of patient fitness (particularly cardiac, respiratory and renal co-morbidities) and technical considerations. ~~Nowadays,~~ EVAR is currently the primary mode of treatment for abdominal aortic aneurysms (AAA), with over 80% of elective cases being performed by endovascular repair(2,3). Nevertheless, EVAR has a significantly higher rate of secondary interventions due to endoprosthesis-related complications as compared to open surgery(4,5). Even though the majority of these complications can be easily managed by endovascular means, a late open conversion (LOC) is sometimes required(3,5).

According to the recent literature, LOC (>30 postoperative days) occurs in 3.7% of patients following EVAR (range: 0.9 – 22.8%)(6). This incidence will likely rise in the future, since the number of patients undergoing EVAR is increasing(6,7). LOC may be associated with higher mortality and morbidity rates compared to primary open repair, as a result of the technical difficulties that may be encountered during the operation, mainly related to the access, the aortic cross-clamping and the stent-graft removal(5,6,8).

In the majority of the series reported in the literature, the abdominal aorta is usually clamped above the endograft, in a suprarenal or supraceliac position(5,6,9). The aim of this study is to assess the feasibility of an infrarenal aortic cross-clamping during LOC after EVAR, by evaluati~~o~~ng the technical aspects and outcomes in our single centre experience.

Materials and Methods

Patients and study design. Records of all patients who underwent LOC in our centre, from January 1996 to October 2016, were collected into a prospective database and analyzed retrospectively. LOC was defined as a total or partial endograft explant at least 30 days after the initial EVAR procedure, followed by reconstruction of the aortic anatomy. Patients who underwent open surgical attempts to repair endoleaks without graft removal (i.e. sacculotomy and lumbar artery ligation) were excluded.

Demographic (sex, age), clinical (cardiovascular risk factors such as hypertension, coronary artery disease (CAD), tobacco smoking, atrial fibrillation, diabetes mellitus, dyslipidaemia), EVAR procedure (date of the implant, device type and characteristics) and surgical data (delay between the initial EVAR and conversion, reason for removal, extent of stent-graft removal, ~~and~~ type of reconstruction, operative time, blood loss and need for transfusions) were obtained for analysis (Table I).

Primary endpoints were: (i) operative technical success and (ii) 30-day mortality and morbidity. Morbidity included acute postoperative kidney injury, hemodialysis (permanent or temporary), arrhythmia, myocardial infarction, respiratory infection, prolonged ventilation or intensive care unit (ICU) stay. Acute kidney injury and renal failure were considered when sudden (1 – 7 days) and sustained (>24 hours), and were based on the RIFLE criteria (more than two-fold increase in serum creatinine from baseline)(10).

In accordance with the Ethical Review Board of our institution, a written informed consent was obtained from all patients except for one who presented with hypovolemic shock.

Indications and surgical technique. Indications for LOC were the presence of a type I or III endoleak, or other types of endoleaks when symptomatic~~s~~ or associated with aneurysmal sac growth ≥1cm/year, not amenable to endovascular repair or after one or more unsuccessful endovascular attempts (i.e. aortic cuff or embolization of a type II endoleak), or if surgical attempts to repair the

endoleak without graft removal was not technically feasible. LOC was indicated also in case of graft failure (such as recurrent limb thrombosis).

All patients underwent a transperitoneal approach through a midline incision. Proximal cross-clamping was infrarenal in all cases (Fig. 1). The proximal stents were completely removed in case the main body of the endograft was not caught by the aortic clamp (e.g. in case of distal migration of the endograft, Fig. 1). Otherwise, the proximal covered stent was used as a "neo-neck", sewing together the Dacron graft, the aortic wall and the endograft (Fig. 2 and 3) in order to minimize the risk of late dilatation of the residual infrarenal aorta and to avoid further complications due to a late migration of the remaining stentgraft(11). The distal portion of the endoprosthesis was preserved in case of apparent incorporation of the graft into the vessel wall(12). Exclusion criteria for this technique were the presence of endograft infection or complete aneurysmal degeneration of the proximal neck with consequential transformation in juxta-renal or thoraco-abdominal aneurysm.

Follow-up. Follow-up was undertaken with clinical and ultrasound examinations at 1 month, 3 months, 6 months and yearly thereafter, assessing the patency of the graft, the status of the anastomoses and patient long-term survival. CT-scan was not performed systematically, but in combination with ultrasounds in selected cases.

Statistics. Data were recorded and tabulated in a Microsoft Excel (Microsoft Corporation, Redmond, Wash, USA) database. Preoperative results are presented as mean ± standard deviation (SD) or median with range for continuous variables, while categorical ones are presented as number (percentage). Peri- and postoperative results in terms of technical success, mortality and renal morbidity were evaluated by Mann-Whitney U test or with the Kruskal-Wallis test (for continuous variables) or with the χ^2 test or Fisher exact test as appropriate (in case of dichotomous variables). Owing to the small number of 30-day and long-term mortality events, multivariate logistic regression analysis was not performed for either outcome. Long-term survival was analyzed by Kaplan-Meier curves. A P value of $<.05$ was considered statistically significant. Statistical analysis was performed with dedicated software (Epi Info 7.0.9.34; CDC, Atlanta, Ga, USA or StatView 5.0;

SAS Institute Inc, Cary, NC, USA).

Results

Demographic data, clinical presentation, indications and endograft characteristics. During the 20-year period of the study, 32 patients underwent open conversion after EVAR. Among these, 4 patients were operated within 30 days from the initial EVAR (early conversions), and were therefore excluded from the analysis. Thus, 28 patients were available for analysis. Mean age at the time of conversion was 75.11 years (SD ± 6.65). Twenty-six out of 28 patients were male (92.86%). The median time between the initial EVAR and the LOC was 41.4 months (range: 5.97 – 112.67 months). Complete data about patients' demographic, risk factors and comorbidities are summarized in Table I.

An elective operation was performed in 21/28 patients (75%). In 7 patients (25%) LOC was performed in an urgent setting; among these, 4 patients presented with a ruptured aneurysm, 2 patients with an abdominal pain related to AAA, and 1 patient with graft failure (recurrent limb thrombosis after 2 endovascular corrections). In 27 patients the indication for LOC was persistent endoleak: 20 type I, 4 type II associated with sac enlargement, 3 type III, and 3 endotensions (defined as sac enlargement in the absence of identifiable endoleak). ~~In 27 patients, indication for LOC was represented by the presence of an endoleak, specifically: 20 patients presented a type I endoleak, 4 patients a type II associated with aneurysm growth, 3 patients a type III endoleak and 3 patients a type IV / endotension (this group was defined as an aneurysm sac enlargement without the evidence of an endoleak on the preoperative CT-scan and intraoperatively).~~ In 3 cases (11.1%) multiple types of endoleak were present (2 cases of type I associated with type II, and 1 case of type II associated with a type III). In one case, LOC was performed for graft failure (recurrent limb thrombosis). We did not experience cases of~~No~~ endograft infection nor complete degeneration of the proximal neck~~underwent LOC~~ in our series. These data are presented in Table II.

The type of removed stentgrafts and their characteristics are summarized in Table III. The grafts were Talent in 9 cases, Endurant in 2 cases and AneuRX (Medtronic, Santa Rosa, CA, USA) in 2 cases, Vanguard (Boston Scientific, Natick, MA, USA) in 5 cases (among these, 2 cases were aortic

tubes), Anaconda (Vascutek, Inchinnan, UK) in 4 cases, Zenith Low Profile (Cook, Bloomington, IN, USA) in 3 cases, Stentor (Mintec, La Ciotat, France) in 2 cases, and Nellix (Endologix, Inc., Irvine, CA, USA) in 1 case. A suprarenal fixation was present in the 75% of the cases, and the proximal stent of the endoprosthesis was equipped with hooks in the 32.1%.

Operative data and early results. Technical success rate was 100%: an infrarenal cross-clamping was possible in all cases, with no need of temporary suprarenal clamp positioning. Complete removal of the endograft was performed in 8/28 cases (28.57%). A partial removal was performed in the remaining 20 cases: in 16/20 patients (80%) the proximal portion of the stent-graft was preserved (Fig. 4), while in 4 cases (20%) we preserved the distal part. In case of partial removal, ~~R~~resection of the ~~stent graft~~endoprosthesis was always performed at the level of the fabric to minimize the risk that a cut metal stent would finally ~~of~~ ero~~sion~~de the new graft or the suture line. Reconstruction were performed with dacron grafts, and included 17 aorto-bi-iliac bypasses, 10 aorto-aortic tubes and 1 aorto-bifemoral bypass. No patient required revascularization of visceral or renal vessels. Mean operative time was 239 ± 80 min. Median estimated blood loss was 1000 mL (range: 500 – 3500 mL). Median transfused red blood cells units during surgery were 0.5 (range: 0 – 6 units).

Overall 30-day mortality was 7.14% (2/28). Thirty-day mortality rate was 9.5% in elective patients and 0% in urgent settings. This difference was not statistically significant (P=.56). These two patients died of multi-organ failure (MOF) during ICU stay, which likely resulted from pulmonary infection secondary to prolonged ventilation. No predictive risk factor of early mortality was found ~~(Table IV)~~.

Early morbidity rate was calculated by excluding postoperative deaths (n=26). Overall systemic morbidity rate was 38.5% (10/26 patients). This included 5 cases of prolonged ventilation and ICU stay >4 days (among these, 2 cases of pneumonia), 2 myocardial infarctions not requiring revascularization, 2 renal injuries, and 1 low-grade large bowel ischaemia not requiring surgical treatment.

Postoperative kidney injury rate was 7.7% (2/26). These patients presented a transient increase in serum creatinine (more than two-fold from baseline), requiring haemodialysis in one case. In this case, serum creatinine was comparable to preoperative values at discharge, and no additional dialysis procedure was subsequently required. ~~The presence of a ruptured aneurysm was a risk factor for postoperative kidney injury~~Only aneurysm rupture predicted postoperative renal dysfunction (P=.02). The presence of a suprarenal fixation of the endograft (P=.47), or the complete vs. partial removal of the endoprosthesis (P=.47) did not affect this endpoint. ~~These data are summarized in Table IV.~~

No significant perioperative surgical complication such as bleeding requiring revision, acute limb ischaemia or bowel injury was registered.

Follow-up data and long-term results. Mean follow-up was 47.37 months ± 55.67 SD (range, 0.23 – 175.07 months); no patient was lost at follow-up. Aortic grafts remained patent during the follow-up, and no anastomotic stenosis nor aneurysm degeneration were recorded. No additional procedure related to aortic complications was performed during follow-up. The survival rate was estimated at 84% at 6 months, 78% at 5 years and 58% at the 10-year follow-up by means of the Kaplan-Meier method (Fig. 5). No aneurysm-related death occurred during follow-up.

Discussion

EVAR offers a clear early survival benefit compared to open repair(13). Furthermore, this minimally invasive technique seems to be preferred by patients(14), and it is currently the method of choice for repair of AAA in Western Countries(9,13). Even though endovascular materials, and planning and imaging methods are constantly improving(13,15), aortas affected by aneurysmal disease may continue to dilate and over time even a modern device could leak or migrate. In fact, according to the most recent literature, LOC is still needed in about 3.7% of patients following EVAR (range: 0.9 – 22.8%)(6). In addition, since the number of patients undergoing EVAR is increasing, the incidence of LOC will likely rise in the future.

Early open conversions (within 30 days after EVAR) are typically the result of technical problems during endograft advancement or deployment (such as renal artery coverage or iliac rupture), or early graft failure (such as thrombosis of the endoprosthesis). Consequently, these procedures are usually carried out in an urgent setting(8,16). On the contrary, LOC are typically associated with aneurysm growth due to endoleaks, stent migration and late limb or graft thrombosis not amenable to endovascular therapy, and are usually carried out in an elective manner(8,16–19). For these reasons, early open conversions were considered as a different entity and were therefore excluded from this analysis. In our series, an elective operation was performed in 75% of the cases, in accordance with the recent review by Kouvelos et al. which indicates a rate of 77.5%(6).

LOC is associated with a considerably increased perioperative morbidity and mortality as compared to standard EVAR or open repair(3). Harris et al. reported, in the EUROSTAR registry, a 24% mortality rate(17). This may be due to several technical issues that can be encountered during this intervention, specifically related to the access, aortic clamping, stent-graft removal and aortic reconstruction(3,8). In addition, a significant number of patients undergoing LOC may have been considered unfit for open surgery at the time of the initial EVAR.

In the great majority of the series reported in the literature, the abdominal aorta is usually clamped above the endograft, in a suprarenal or supraceliac position. Wu et al. report a 74% rate of

suprarenal aortic clamping, Turney et al. 87%, and in the recent review by Kouvelos et al. the cross-clamping site was above the renal arteries in 56% (316/566) of the cases(5,6). The rationale is to avoid direct endograft clamping, because of the possibility that this manoeuvre may lead to stent-structure damage and/or aortic mechanical lesions. On the contrary, suprarenal cross-clamp was identified as a risk factor for 30-day mortality in the series published by Scali et al(20). Moreover, patients undergoing suprarenal aortic cross-clamping tend to develop a higher rate of visceral ischaemia compared to patients undergoing infrarenal clamping(2.3 vs. 0.8%)(21). Furthermore, a prolonged suprarenal or celiac clamping, which may be necessary in complex LOC, are associated with a higher risk of postoperative renal injury, especially in patients with preoperative renal insufficiency(22,23). In addition, in case of a well incorporated endoprosthesis with suprarenal fixation, cannulation of the ~~visceral and~~ renal arteries for ~~renal~~ protection by cristalloid perfusion may be difficult or even impossible to perform due to the presence of the bare metal stent at the level of the target arteries~~suprarenal free-flow~~(8,24,25).

In our series, the abdominal aorta was always clamped in an infrarenal position, regardless of the presence and the characteristics of the proximal part of the endograft. Despite some Authors reported that an infrarenal clamping may be impossible as a result of chronic inflammation in the neck area, in our experience this was feasible in all cases, as demonstrated by a technical success rate of 100%(5,11). We did not experience stent-structure damages or aortic mechanical lesions (dissections or intra- or post-operative bleeding) as a result of the direct endograft clamping (Fig. 4). In our series, overall 30-day mortality was 7.14%, in accordance with the recent literature: Ultee et al. report a mortality rate of 10% in their series(3). We experienced no differences in 30-day mortality rate when we compared the subgroup of patients who underwent elective repair vs. urgent patients (P=.56). This is in contrast with reports of an early mortality of 3.2% among elective patients vs. 29.2% among non-elective cases(6). ~~Currently, we are not able to explain this difference.~~ However, this discrepancy may be related to the small number of urgent patients in our series.

One of the major complication of LOC is ~~represented by~~ aortic or renal dissection or occlusion that may occur during complete proximal removal of the endograft, particularly when the device is well incorporated in the aortic wall. Marone et al. experienced a 24% acute renal failure rate in their series, requiring urgent angiography and renal artery stenting in 3/13 cases (in one case, only one kidney was revascularized and the patient needed postoperative temporary hemodialysis)(8). Furthermore, Turney et al. reported renal failure requiring hemodialysis only among patients experiencing supraceliac clamp(9). In our series, we recorded 7.7% temporary postoperative kidney injury rate, and no surgical or endovascular renal revascularization was needed. The only risk factor for acute renal failure was a ruptured aneurysm with hemorrhagic shock at presentation (P=.02). The presence of a suprarenal fixation of the endograft did not affect this endpoint. For these reasons, we suggest a complete endoprosthesis removal only in case of graft infection. However, we did not experienced such events in our series.

Bonvini et al. proposed a “neo-neck” technique for proximal anastomosis with preservation of the first covered stent during LOC for EVAR with suprarenal fixation(11). Nevertheless, with this technique, the aorta is always occluded in a supraceliac position (with a clamp or an aortic balloon), and the cross-clamping site is moved in an infrarenal position only after the completion of the proximal anastomosis, exposing to visceral and renal ischaemia. Furthermore, visceral and renal perfusion is precluded by the presence of the aortic balloon. By using an exclusively infrarenal cross-clamping technique, the preservation of the proximal stent is feasible, avoiding supra-renal clamping. In fact, a suprarenal fixation of the endograft was present in the 75% of the cases in our series, and the proximal part of the endoprosthesis was preserved in 16 patients (57%). In this setting, LOC was performed in all cases and did not require temporary suprarenal clamping.

Overall early systemic morbidity rate was 38.5% in our series, which was not surprising given the well-known frailty of this patient population and the technical difficulties of LOC. The 5 cases requiring prolonged ventilation and ICU stay confirm that these patients suffer from important preoperative comorbidities, and suggest that these patients may have been considered unfit for open

surgery at the time of the initial EVAR. These complications resolved before discharge, and we did not experience significant perioperative surgical complication such as bleeding requiring revision, acute limb ischaemia or bowel injury needing operative management.

Despite the potential limitations of a retrospective analysis, the present study evaluates for first the outcomes of LOC by solely using an infrarenal clamp position. Indeed, current literature is based on only suprarenal or both suprarenal and infrarenal aortic cross-clamping site. A potential limitation of this technique may be related to its ~~low feasibility~~ lack of applicability in cases of complete aneurysmal degeneration of the proximal aortic neck with subsequent ~~de facto transformation~~development of a ~~in~~ juxta-renal, para-renal or thoraco-abdominal aneurysm. In this case, we ~~suggest to take into consideration~~recommend ~~an~~ endovascular therapy using a fenestrated or branched endograft, or an open conversion where the aortic cross-clamping is performed in an healthy proximal site of the aorta. Finally, we did not experience stent-graft infections in our series. In this case, a complete explantation of the endoprosthesis is mandatory.

To the best of our knowledge, our follow-up of LOC is the longest ever published in literature, reaching a peak of 175.07 months(5,6). Despite a higher early mortality rate, the survival rate of 78% at the 5-year follow-up, which is in accordance with the main randomized controlled trial, indicates that LOC with infrarenal clamping of the endograft is a safe and feasible procedure which carries a late survival benefit(2,13). This is supported by the fact that no additional procedure related to aortic complications was performed during the mean follow-up of 47.37 months, and no aneurysm-related death occurred.

Conclusions

According to the current literature, the incidence of endograft failure without further options for endovascular salvage keeps rising significantly(6). Explant results are associated with morbidity and mortality rates that may exceed those found for elective primary repair, due to the technical difficulties that are encountered during LOC and the high surgical risk that characterize this subgroup of patients.

LOC after EVAR with infrarenal clamping of the endograft demonstrated to be a feasible, safe and effective technique, with satisfactory post-operative mortality and morbidity rates. This method, in properly selected patients, allows to simplify the surgical technique, and potentially avoids renal and visceral complications that may be related to a suprarenal or supraceliac clamping.

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Figure 1

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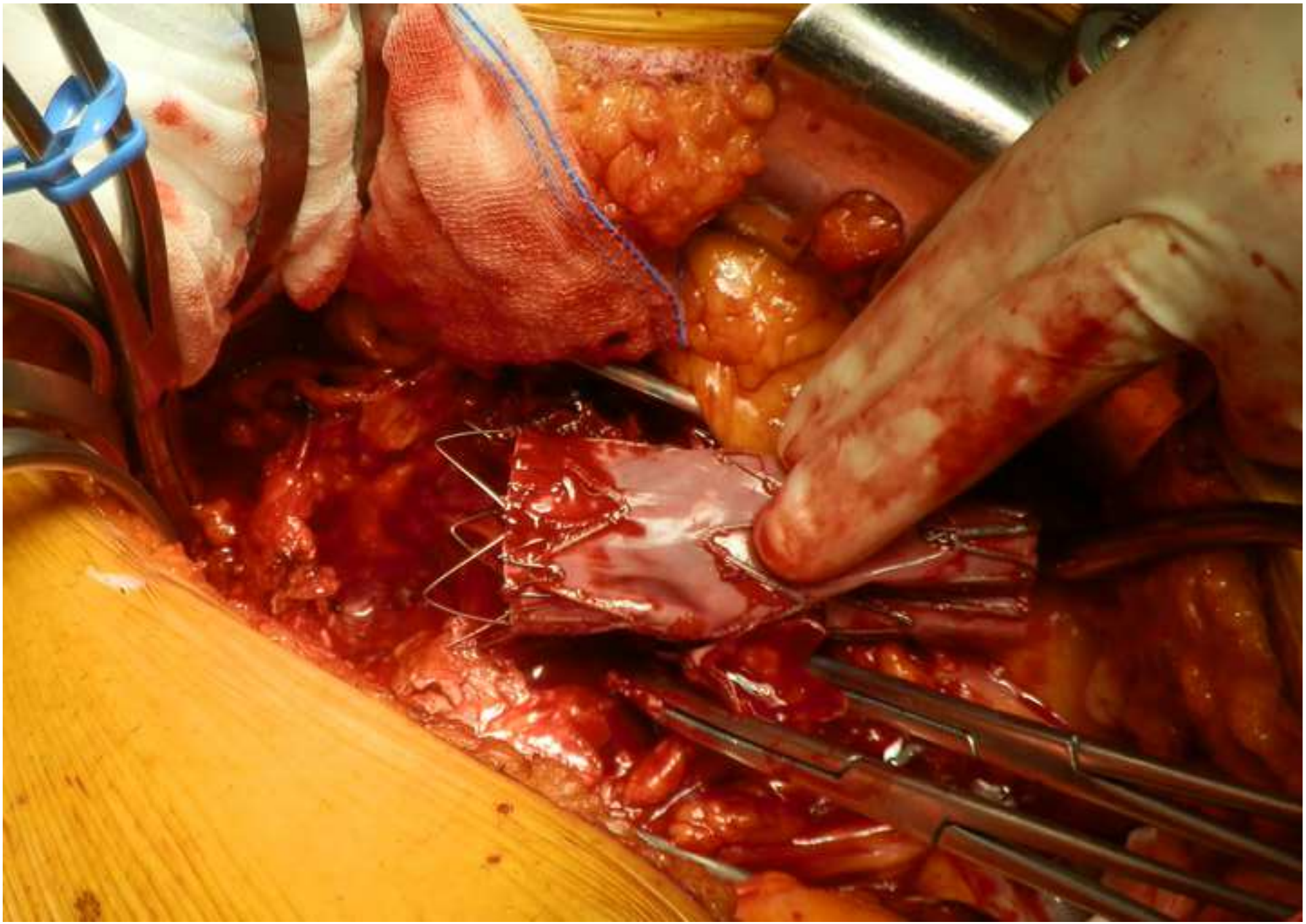

Figure 2

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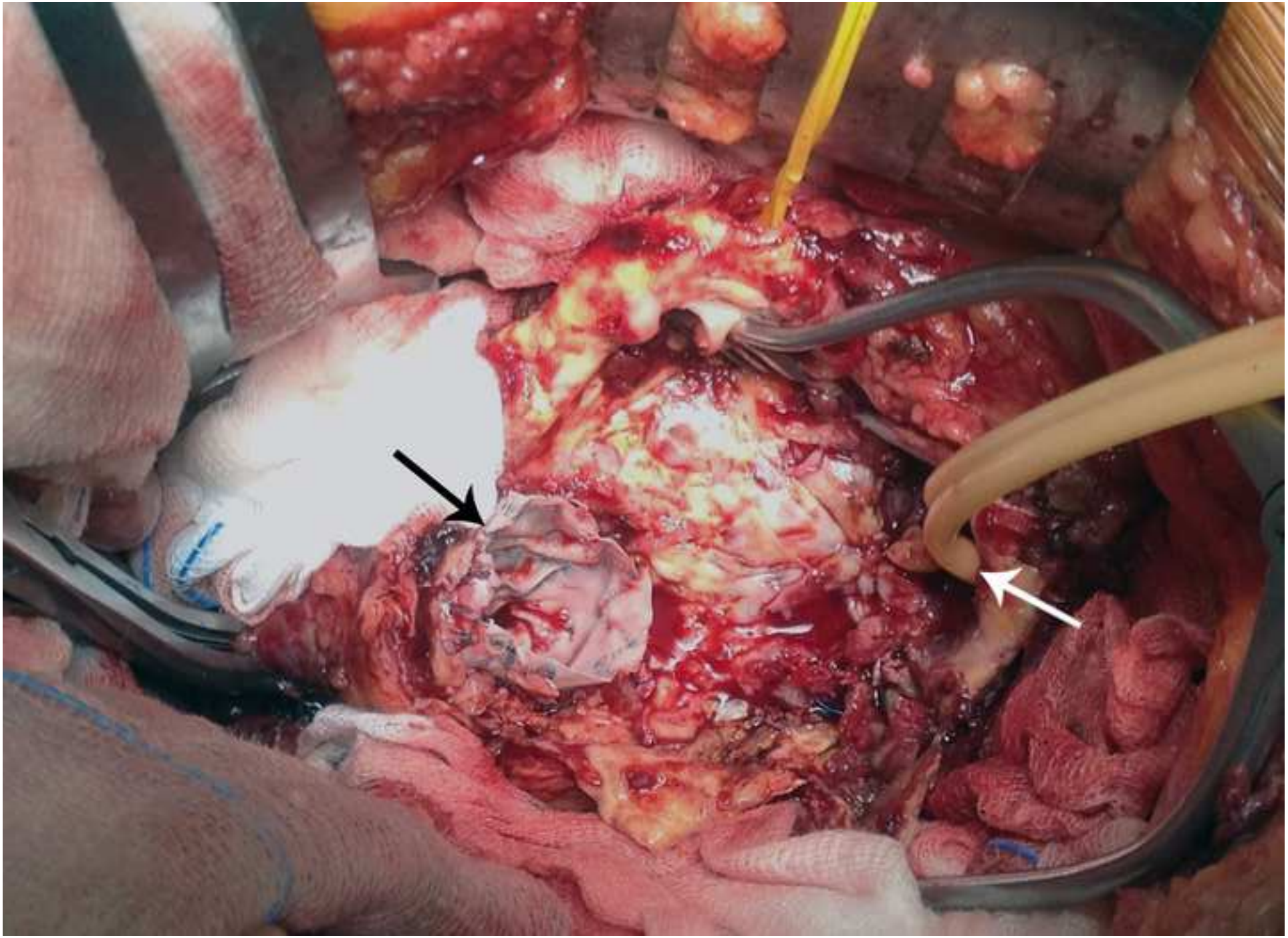

Figure 3

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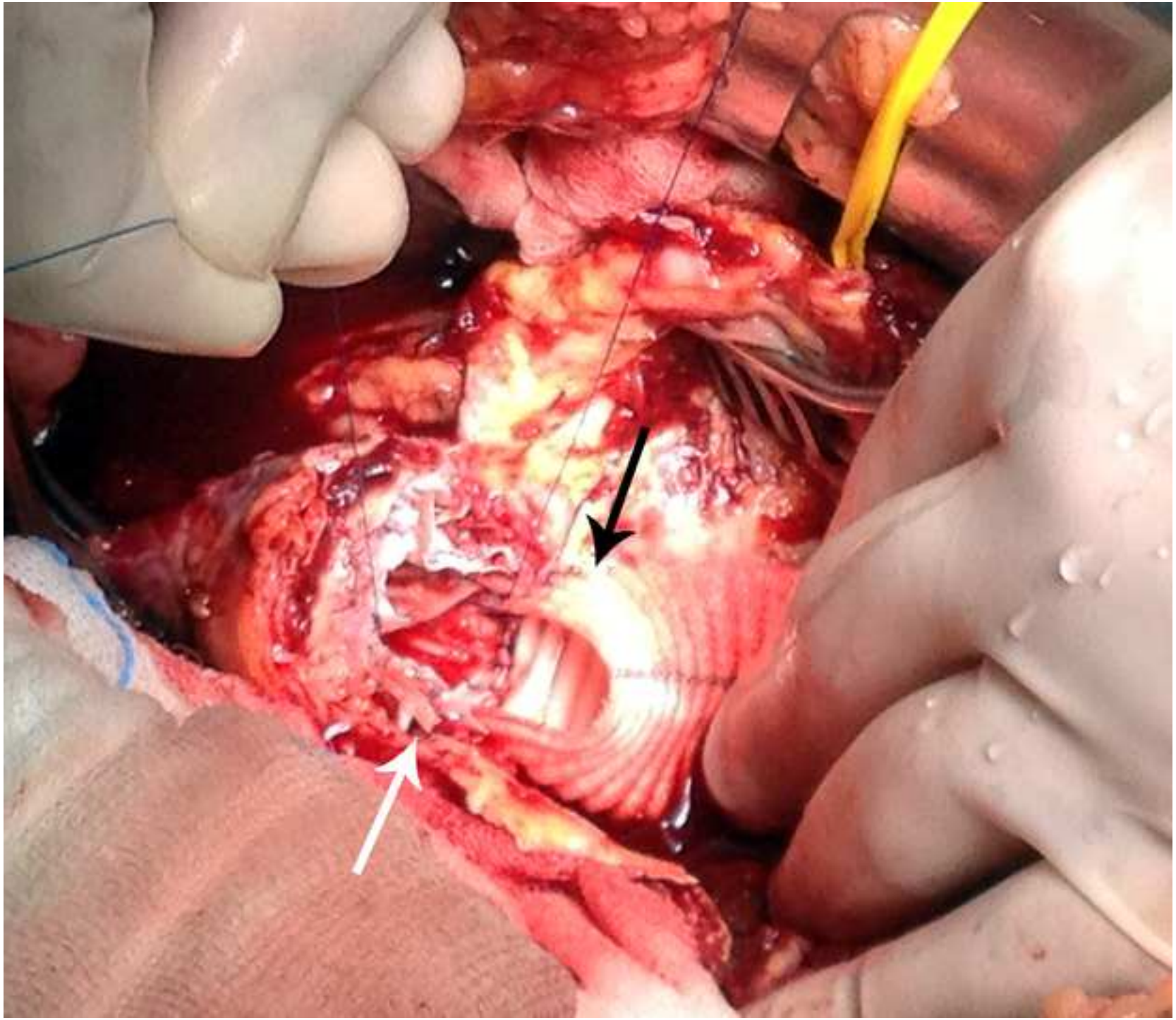


Figure 4a

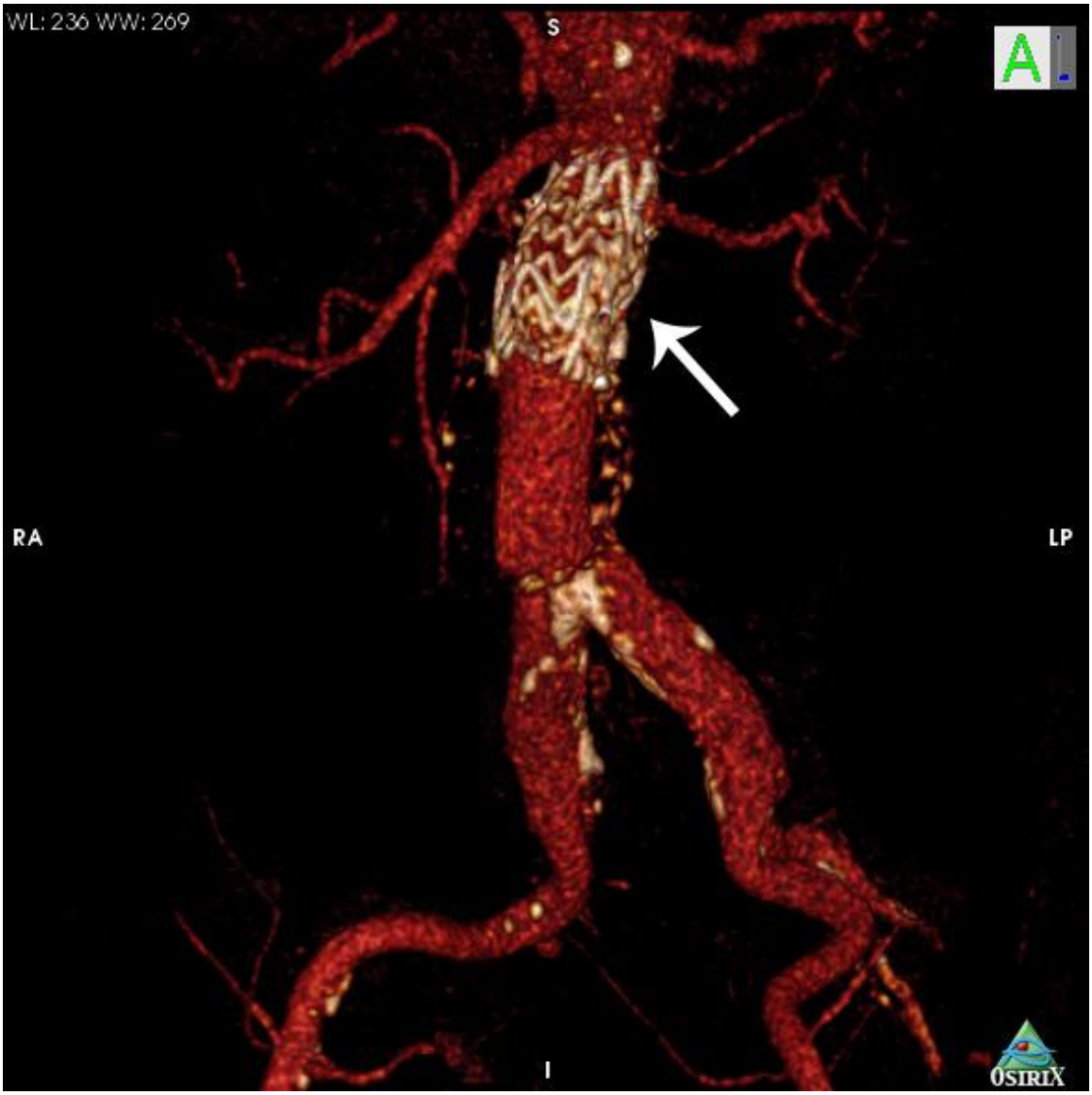


Figure 4b

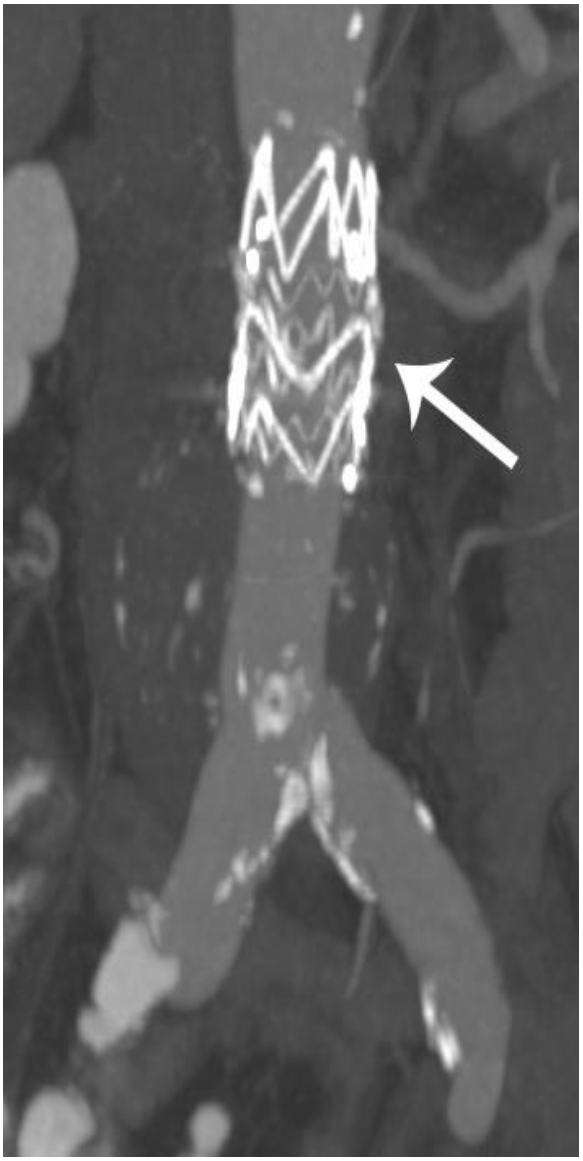
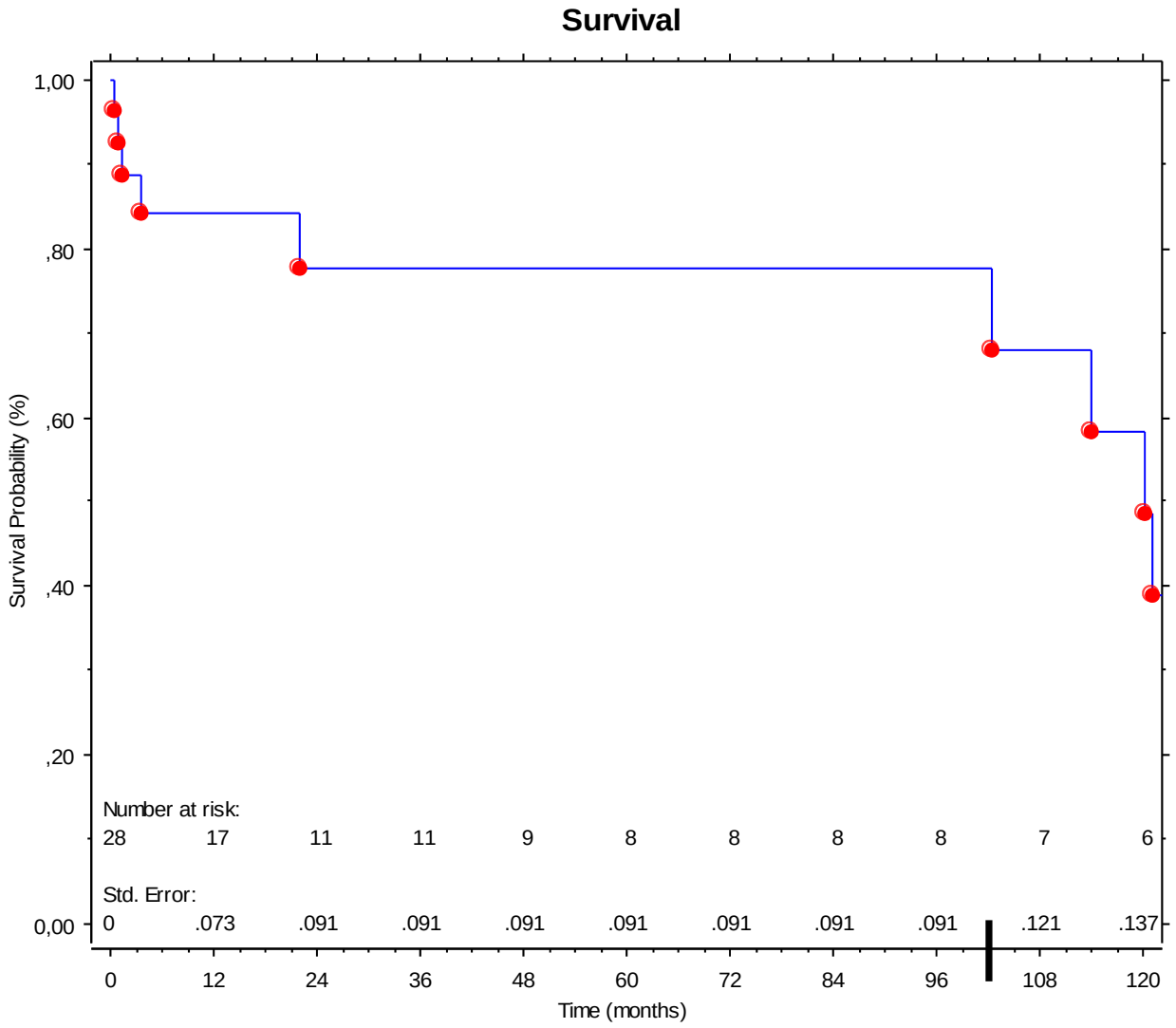


Figure 5


Survival
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Survival Probability (%)
Number at risk:
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Std. Error:
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0 12 24 36 48 60 72 84 96 108 120
Time (months)

Table I. Preoperative data of patients undergoing LOC.

Variables	**n=28**
Age at EVAR, years	71.39 ± 6.32
Age at conversion, years	75.11 ± 6.65
Male sex	26 (92.9%)
Risk factors	
Renal insufficiency (pre-existing)[a]	7 (25%)
Smoking (ongoing)	12 (42.9%)
COPD	19 (67.9%)
Hypertension	28 (100%)
Diabetes mellitus	2 (7.1%)
CAD	13 (46.4%)
Atrial fibrillation	9 (32.1%)
Dyslipidaemia	10 (37%)
ASA score	
ASA 2	5 (17.9%)
ASA 3	19 (67.9%)
ASA 4	4 (14.3%)
LOC delay, median (range) months[b]	41.4 (5.97 – 112.67)

LOC, late open conversion; EVAR, endovascular aneurysm repair; COPD, chronic obstructive pulmonary disease; CAD, Coronary Artery Disease; ASA, American Society of Anesthesiologists
Continuous data are presented as mean ± standard deviation and categoric data as number (%).
[a]Pre-existing renal insufficiency is defined as serum creatinine ≥ 1.5mg/dL.
[B]LOC delay is defined as the delay between the initial EVAR and open conversion.

Table II. Indications for conversion.

Indication	**n (%)**
Endoleak	27/28 (96.4%)
Type I	20/27 (74.1%)
Type II	4/27 (14.8%)
Type III	3/27 (11.1%)
Endotension	3/27 (11.1%)
Multiple[a]	3/27 (11.1%)
Graft failure[b]	1/28 (3.6%)
Urgent setting[c]	7/28 (25%)
Rupture	4/28 (14.3%)

[a]Multiple endoleaks: 2 cases of type I endoleak associated with a type II, and 1 case of type II associated with a type III.
[b]Recurrent limb thrombosis.
[c]Urgent setting included ruptured aneurysms (4 patients) and symptomatic patients (3 patients: 2 abdominal pain and 1 graft failure)

Table III. Types and characteristics of the removed stent-grafts.

Stent-graft type	**n=28 (%)**
Talent, Medtronic	9 (32.1%)
Vanguard, Boston Scientific	5 (17.9%)
Anaconda, Vascutek	4 (14.3%)
Zenith Low Profile, Cook	3 (10.7%)
Endurant, Medtronic	2 (7.1%)
AneuRX, Medtronic	2 (7.1%)
Stentor, MinTec	2 (7.1%)
Nellix, Endologix	1 (3.6%)
Fixation	
Suprarenal	21 (75%)
Infrarenal	7 (25%)
Presence of hooks	
Yes	9 (32.1%)
No	19 (67.9%)

All endografts were bifurcated except 2 Vanguard aortic tubes.

Legends of figures

Figure 1. Complete removal of the proximal part of the endograft. In this case, the Talent endoprosthesis migrated distally, so it was not caught by the clamp and the removal could be easily performed.

Figure 2. Partial removal of the endograft (proximal preservation). In this case, the endograft with a suprarenal fixation and hooks was clamped and cut at the level of the fabric (black arrow). The distal part was removed. The iliac arteries were clamped endoluminally with Foley catheters (white arrow).

Figure 3. Proximal anastomosis. The Dacron graft (black arrow), the endograft and the aortic wall (white arrow) are sewn together.

Figure 4. Postoperative CT scan (a. 3D-Volume Rendering reconstruction; b. Maximum Intensity Projection) showing the preservation of the proximal part of the endograft (including the suprarenal bare stent) in an aorto-aortic reconstruction with a Dacron tube graft in a patient with a pre-existing solitary kidney. The clamping of the endograft did not affect or damage its structure. The arrow depicts the site of the proximal anastomosis. Patient n. 27, Medtronic Talent bifurcated endograft + Medtronic Endurant cuff positioned for a type I endoleak, explanted after 65 months from the initial EVAR for a type III endoleak.

Figure 5. Ten-years estimated survival for the patients who underwent late open conversion after EVAR. Standard error exceeds 10% after 102 months of follow-up.

Title: Infrarenal endograft clamping in late open conversions after endovascular abdominal aneurysm repair

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Abstract and key words

Objective. The aim of this study is to report the technical aspects and outcomes of late open conversions (LOC) after endovascular aneurysm repair (EVAR) in a single centre, by using exclusively infrarenal clamping of the endograft as an alternative to suprarenal or supraceliac aortic clamping.

Materials and Methods. A retrospective analysis of EVAR requiring late explants (>30 days) from January 1996 to October 2016 was performed. Patients' demographics, type of endograft, duration of implant, reason for removal, extent of stent-graft removal, type of reconstruction, 30-day mortality, postoperative complications and log-term survival were obtained for analysis.

Results. During the study period, 28 patients required LOC. The mean age at conversion was 75.11 years ± 6.65; 26/28 (92.86%) were male. Grafts were excised after a median of 41.4 months (range, 5.97 – 112.67 months), with 21/28 explants (75%) performed electively. Multiple types of EVAR devices have been explanted: suprarenal fixation was present in the 75% of the cases. Indication for LOC was the presence of an endoleak in 27 cases (20 type I, 4 type II associated with aneurysm growth, 3 type III, 3 endotensions; in 3 cases multiple types of endoleak were present) and graft thrombosis in 1 case. All patients underwent transperitoneal approach with infrarenal clamping. No patient required revascularization of visceral or renal vessels. Complete removal of the stentgraft was performed in 8/28 cases, partial removal in the remaining 20 cases (with conservation of the proximal portion in 16/20 cases). Technical success was 100%. Overall 30-day mortality was 7.14% (2/28). Thirty-day mortality was 9.5% in elective patients, and 0% in urgent setting; this difference was not statistically significant (p=.56). Postoperative kidney injury rate was 7.7% (2/26). Mean follow-up was 47.37 months ± 55.67 SD (range, 0.23 – 175.07 months). The estimated 5-year survival rate was 78%. No aneurysm-related death nor additional procedure occurred during follow-up.

Conclusions. LOC after EVAR using the infrarenal clamping of the endograft is a feasible and effective technique, with satisfactory post-operative mortality and morbidity. This method allows

simplifying the surgical technique, and may avoid renal and visceral complications related to a suprarenal or supraceliac clamping.

Key words: abdominal aortic aneurysm, open surgical conversion, endovascular repair, EVAR, late complications

Text

Introduction

Since the initial description by Parodi in 1991[1], endovascular aneurysm repair (EVAR) has gained widespread acceptance. In the current vascular practice, the selection of endovascular surgery for aneurysm repair is based upon both the assessment of patient fitness (particularly cardiac, respiratory and renal co-morbidities) and technical considerations. EVAR is currently the primary mode of treatment for abdominal aortic aneurysms (AAA), with over 80% of elective cases being performed by endovascular repair[2,3]. Nevertheless, EVAR has a significantly higher rate of secondary interventions due to endoprosthesis-related complications as compared to open surgery[4,5]. Even though the majority of these complications can be easily managed by endovascular means, a late open conversion (LOC) is sometimes required[3,5].

According to the recent literature, LOC (>30 postoperative days) occurs in 3.7% of patients following EVAR (range: 0.9 – 22.8%)[6]. This incidence will likely rise in the future, since the number of patients undergoing EVAR is increasing[6,7]. LOC may be associated with higher mortality and morbidity rates compared to primary open repair, as a result of the technical difficulties that may be encountered during the operation, mainly related to the access, the aortic cross-clamping and the stent-graft removal[5,6,8].

In the majority of the series reported in the literature, the abdominal aorta is usually clamped above the endograft, in a suprarenal or supraceliac position[5,6,9]. The aim of this study is to assess the feasibility of an infrarenal aortic cross-clamping during LOC after EVAR, by evaluating the technical aspects and outcomes in our single centre experience.

Materials and Methods

Patients and study design. Records of all patients who underwent LOC in our centre, from January 1996 to October 2016, were collected into a prospective database and analyzed retrospectively. LOC was defined as a total or partial endograft explant at least 30 days after the initial EVAR procedure, followed by reconstruction of the aortic anatomy. Patients who underwent open surgical attempts to repair endoleaks without graft removal (i.e. sacculotomy and lumbar artery ligation) were excluded.

Demographic (sex, age), clinical (cardiovascular risk factors such as hypertension, coronary artery disease (CAD), tobacco smoking, atrial fibrillation, diabetes mellitus, dyslipidaemia), EVAR procedure (date of the implant, device type and characteristics) and surgical data (delay between the initial EVAR and conversion, reason for removal, extent of stent-graft removal, type of reconstruction, operative time, blood loss and need for transfusions) were obtained for analysis (Table I).

Primary endpoints were: (i) operative technical success and (ii) 30-day mortality and morbidity. Morbidity included acute postoperative kidney injury, hemodialysis (permanent or temporary), arrhythmia, myocardial infarction, respiratory infection, prolonged ventilation or intensive care unit (ICU) stay. Acute kidney injury and renal failure were considered when sudden (1 – 7 days) and sustained (>24 hours), and were based on the RIFLE criteria (more than two-fold increase in serum creatinine from baseline)[10].

In accordance with the Ethical Review Board of our institution, a written informed consent was obtained from all patients except for one who presented with hypovolemic shock.

Indications and surgical technique. Indications for LOC were the presence of a type I or III endoleak, or other types of endoleaks when symptomatic or associated with aneurysmal sac growth ≥1cm/year, not amenable to endovascular repair or after one or more unsuccessful endovascular attempts (i.e. aortic cuff or embolization of a type II endoleak), or if surgical attempts to repair the

endoleak without graft removal was not technically feasible. LOC was indicated also in case of graft failure (such as recurrent limb thrombosis).

All patients underwent a transperitoneal approach through a midline incision. Proximal cross-clamping was infrarenal in all cases (Fig. 1). The proximal stents were completely removed in case the main body of the endograft was not caught by the aortic clamp (e.g. in case of distal migration of the endograft, Fig. 1). Otherwise, the proximal covered stent was used as a "neo-neck", sewing together the Dacron graft, the aortic wall and the endograft (Fig. 2 and 3) in order to minimize the risk of late dilatation of the residual infrarenal aorta and to avoid further complications due to a late migration of the remaining stentgraft[11]. The distal portion of the endoprosthesis was preserved in case of apparent incorporation of the graft into the vessel wall[12]. Exclusion criteria for this technique were the presence of endograft infection or complete aneurysmal degeneration of the proximal neck with consequential transformation in juxta-renal or thoraco-abdominal aneurysm.

Follow-up. Follow-up was undertaken with clinical and ultrasound examinations at 1 month, 3 months, 6 months and yearly thereafter, assessing the patency of the graft, the status of the anastomoses and patient long-term survival. CT-scan was not performed systematically, but in combination with ultrasounds in selected cases.

Statistics. Data were recorded and tabulated in a Microsoft Excel (Microsoft Corporation, Redmond, Wash, USA) database. Preoperative results are presented as mean ± standard deviation (SD) or median with range for continuous variables, while categorical ones are presented as number (percentage). Peri- and postoperative results in terms of technical success, mortality and renal morbidity were evaluated by Mann-Whitney U test or with the Kruskal-Wallis test (for continuous variables) or with the χ^2 test or Fisher exact test as appropriate (in case of dichotomous variables). Owing to the small number of 30-day and long-term mortality events, multivariate logistic regression analysis was not performed for either outcome. Long-term survival was analyzed by Kaplan-Meier curves. A P value of <.05 was considered statistically significant. Statistical analysis was performed with dedicated software (Epi Info 7.0.9.34; CDC, Atlanta, Ga, USA or StatView 5.0;

SAS Institute Inc, Cary, NC, USA).

Results

Demographic data, clinical presentation, indications and endograft characteristics. During the 20-year period of the study, 32 patients underwent open conversion after EVAR. Among these, 4 patients were operated within 30 days from the initial EVAR (early conversions), and were therefore excluded from the analysis. Thus, 28 patients were available for analysis. Mean age at the time of conversion was 75.11 years (SD ± 6.65). Twenty-six out of 28 patients were male (92.86%). The median time between the initial EVAR and the LOC was 41.4 months (range: 5.97 – 112.67 months). Complete data about patients' demographic, risk factors and comorbidities are summarized in Table I.

An elective operation was performed in 21/28 patients (75%). In 7 patients (25%) LOC was performed in an urgent setting; among these, 4 patients presented with a ruptured aneurysm, 2 patients with an abdominal pain related to AAA, and 1 patient with graft failure (recurrent limb thrombosis after 2 endovascular corrections). In 27 patients the indication for LOC was persistent endoleak: 20 type I, 4 type II associated with sac enlargement, 3 type III, and 3 endotensions (defined as sac enlargement in the absence of identifiable endoleak). In 3 cases (11.1%) multiple types of endoleak were present (2 cases of type I associated with type II, and 1 case of type II associated with a type III). In one case, LOC was performed for graft failure (recurrent limb thrombosis). We did not experience cases of endograft infection nor complete degeneration of the proximal neckin our series. These data are presented in Table II.

The type of removed stentgrafts and their characteristics are summarized in Table III. The grafts were Talent in 9 cases, Endurant in 2 cases and AneuRX (Medtronic, Santa Rosa, CA, USA) in 2 cases, Vanguard (Boston Scientific, Natick, MA, USA) in 5 cases (among these, 2 cases were aortic tubes), Anaconda (Vascutek, Inchinnan, UK) in 4 cases, Zenith Low Profile (Cook, Bloomington, IN, USA) in 3 cases, Stentor (Mintec, La Ciotat, France) in 2 cases, and Nellix (Endologix, Inc., Irvine, CA, USA) in 1 case. A suprarenal fixation was present in the 75% of the cases, and the proximal stent of the endoprosthesis was equipped with hooks in the 32.1%.

Operative data and early results. Technical success rate was 100%: an infrarenal cross-clamping was possible in all cases, with no need of temporary suprarenal clamp positioning. Complete removal of the endograft was performed in 8/28 cases (28.57%). A partial removal was performed in the remaining 20 cases: in 16/20 patients (80%) the proximal portion of the stent-graft was preserved (Fig. 4), while in 4 cases (20%) we preserved the distal part. In case of partial removal, resection of the endoprosthesis was always performed at the level of the fabric to minimize the risk that a cut metal stent would finally erode the new graft or the suture line. Reconstruction were performed with dacron grafts, and included 17 aorto-bi-iliac bypasses, 10 aorto-aortic tubes and 1 aorto-bifemoral bypass. No patient required revascularization of visceral or renal vessels. Mean operative time was 239 ± 80 min. Median estimated blood loss was 1000 mL (range: 500 – 3500 mL). Median transfused red blood cells units during surgery were 0.5 (range: 0 – 6 units).

Overall 30-day mortality was 7.14% (2/28). Thirty-day mortality rate was 9.5% in elective patients and 0% in urgent settings. This difference was not statistically significant (P=.56). These two patients died of multi-organ failure (MOF) during ICU stay, which likely resulted from pulmonary infection secondary to prolonged ventilation. No predictive risk factor of early mortality was found.

Early morbidity rate was calculated by excluding postoperative deaths (n=26). Overall systemic morbidity rate was 38.5% (10/26 patients). This included 5 cases of prolonged ventilation and ICU stay >4 days (among these, 2 cases of pneumonia), 2 myocardial infarctions not requiring revascularization, 2 renal injuries, and 1 low-grade large bowel ischaemia not requiring surgical treatment.

Postoperative kidney injury rate was 7.7% (2/26). These patients presented a transient increase in serum creatinine (more than two-fold from baseline), requiring haemodialysis in one case. In this case, serum creatinine was comparable to preoperative values at discharge, and no additional dialysis procedure was subsequently required. Only aneurysm rupture predicted postoperative renal dysfunction (P=.02). The presence of a suprarenal fixation of the endograft (P=.47), or the complete vs. partial removal of the endoprosthesis (P=.47) did not affect this endpoint.

No significant perioperative surgical complication such as bleeding requiring revision, acute limb ischaemia or bowel injury was registered.

Follow-up data and long-term results. Mean follow-up was 47.37 months ± 55.67 SD (range, 0.23 – 175.07 months); no patient was lost at follow-up. Aortic grafts remained patent during the follow-up, and no anastomotic stenosis nor aneurysm degeneration were recorded. No additional procedure related to aortic complications was performed during follow-up. The survival rate was estimated at 84% at 6 months, 78% at 5 years and 58% at the 10-year follow-up by means of the Kaplan-Meier method (Fig. 5). No aneurysm-related death occurred during follow-up.

Discussion

EVAR offers a clear early survival benefit compared to open repair[13]. Furthermore, this minimally invasive technique seems to be preferred by patients[14], and it is currently the method of choice for repair of AAA in Western Countries[9,13]. Even though endovascular materials, and planning and imaging methods are constantly improving[13,15], aortas affected by aneurysmal disease may continue to dilate and over time even a modern device could leak or migrate. In fact, according to the most recent literature, LOC is still needed in about 3.7% of patients following EVAR (range: 0.9 – 22.8%)[6]. In addition, since the number of patients undergoing EVAR is increasing, the incidence of LOC will likely rise in the future.

Early open conversions (within 30 days after EVAR) are typically the result of technical problems during endograft advancement or deployment (such as renal artery coverage or iliac rupture), or early graft failure (such as thrombosis of the endoprosthesis). Consequently, these procedures are usually carried out in an urgent setting[8,16]. On the contrary, LOC are typically associated with aneurysm growth due to endoleaks, stent migration and late limb or graft thrombosis not amenable to endovascular therapy, and are usually carried out in an elective manner[8,16-19]. For these reasons, early open conversions were considered as a different entity and were therefore excluded from this analysis. In our series, an elective operation was performed in 75% of the cases, in accordance with the recent review by Kouvelos et al. which indicates a rate of 77.5%[6].

LOC is associated with a considerably increased perioperative morbidity and mortality as compared to standard EVAR or open repair[3]. Harris et al. reported, in the EUROSTAR registry, a 24% mortality rate[17]. This may be due to several technical issues that can be encountered during this intervention, specifically related to the access, aortic clamping, stent-graft removal and aortic reconstruction[3,8]. In addition, a significant number of patients undergoing LOC may have been considered unfit for open surgery at the time of the initial EVAR.

In the great majority of the series reported in the literature, the abdominal aorta is usually clamped above the endograft, in a suprarenal or supraceliac position. Wu et al. report a 74% rate of

suprarenal aortic clamping, Turney et al. 87%, and in the recent review by Kouvelos et al. the cross-clamping site was above the renal arteries in 56% (316/566) of the cases[5,6]. The rationale is to avoid direct endograft clamping, because of the possibility that this manoeuvre may lead to stent-structure damage and/or aortic mechanical lesions. On the contrary, suprarenal cross-clamp was identified as a risk factor for 30-day mortality in the series published by Scali et al[20]. Moreover, patients undergoing suprarenal aortic cross-clamping tend to develop a higher rate of visceral ischaemia compared to patients undergoing infrarenal clamping(2.3 vs. 0.8%)[21]. Furthermore, a prolonged suprarenal or celiac clamping, which may be necessary in complex LOC, are associated with a higher risk of postoperative renal injury, especially in patients with preoperative renal insufficiency[22,23]. In addition, in case of a well incorporated endoprosthesis with suprarenal fixation, cannulation of the renal arteries for protection by cristalloid perfusion may be difficult or even impossible to perform due to the presence of the bare metal stent at the level of the target arteries[8,24,25].

In our series, the abdominal aorta was always clamped in an infrarenal position, regardless of the presence and the characteristics of the proximal part of the endograft. Despite some Authors reported that an infrarenal clamping may be impossible as a result of chronic inflammation in the neck area, in our experience this was feasible in all cases, as demonstrated by a technical success rate of 100%[5,11]. We did not experience stent-structure damages or aortic mechanical lesions (dissections or intra- or post-operative bleeding) as a result of the direct endograft clamping (Fig. 4). In our series, overall 30-day mortality was 7.14%, in accordance with the recent literature: Ultee et al. report a mortality rate of 10% in their series[3]. We experienced no differences in 30-day mortality rate when we compared the subgroup of patients who underwent elective repair vs. urgent patients (P=.56). This is in contrast with reports of an early mortality of 3.2% among elective patients vs. 29.2% among non-elective cases[6]. However, this discrepancy may be related to the small number of urgent patients in our series.

One of the major complication of LOC is aortic or renal dissection or occlusion that may occur

during complete proximal removal of the endograft, particularly when the device is well incorporated in the aortic wall. Marone et al. experienced a 24% acute renal failure rate in their series, requiring urgent angiography and renal artery stenting in 3/13 cases (in one case, only one kidney was revascularized and the patient needed postoperative temporary hemodialysis)[8]. Furthermore, Turney et al. reported renal failure requiring hemodialysis only among patients experiencing supraceliac clamp[9]. In our series, we recorded 7.7% temporary postoperative kidney injury rate, and no surgical or endovascular renal revascularization was needed. The only risk factor for acute renal failure was a ruptured aneurysm with hemorrhagic shock at presentation (P=.02). The presence of a suprarenal fixation of the endograft did not affect this endpoint. For these reasons, we suggest a complete endoprosthesis removal only in case of graft infection. However, we did not experienced such events in our series.

Bonvini et al. proposed a "neo-neck" technique for proximal anastomosis with preservation of the first covered stent during LOC for EVAR with suprarenal fixation[11]. Nevertheless, with this technique, the aorta is always occluded in a supraceliac position (with a clamp or an aortic balloon), and the cross-clamping site is moved in an infrarenal position only after the completion of the proximal anastomosis, exposing to visceral and renal ischaemia. Furthermore, visceral and renal perfusion is precluded by the presence of the aortic balloon. By using an exclusively infrarenal cross-clamping technique, the preservation of the proximal stent is feasible, avoiding supra-renal clamping. In fact, a suprarenal fixation of the endograft was present in the 75% of the cases in our series, and the proximal part of the endoprosthesis was preserved in 16 patients (57%). In this setting, LOC was performed in all cases and did not require temporary suprarenal clamping.

Overall early systemic morbidity rate was 38.5% in our series, which was not surprising given the well-known frailty of this patient population and the technical difficulties of LOC. The 5 cases requiring prolonged ventilation and ICU stay confirm that these patients suffer from important preoperative comorbidities, and suggest that these patients may have been considered unfit for open surgery at the time of the initial EVAR. These complications resolved before discharge, and we did

not experience significant perioperative surgical complication such as bleeding requiring revision, acute limb ischaemia or bowel injury needing operative management.

Despite the potential limitations of a retrospective analysis, the present study evaluates for first the outcomes of LOC by solely using an infrarenal clamp position. Indeed, current literature is based on only suprarenal or both suprarenal and infrarenal aortic cross-clamping site. A potential limitation of this technique may be related to its lack of applicability in cases of complete aneurysmal degeneration of the proximal aortic neck with subsequent development of a juxtarenal, pararenal or thoracoabdominal aneurysm. In this case, we recommend endovascular therapy using a fenestrated or branched endograft, or an open conversion where the aortic cross-clamping is performed in an healthy proximal site of the aorta. Finally, we did not experience stent-graft infections in our series. In this case, a complete explantation of the endoprosthesis is mandatory.

To the best of our knowledge, our follow-up of LOC is the longest ever published in literature, reaching a peak of 175.07 months[5,6]. Despite a higher early mortality rate, the survival rate of 78% at the 5-year follow-up, which is in accordance with the main randomized controlled trial, indicates that LOC with infrarenal clamping of the endograft is a safe and feasible procedure which carries a late survival benefit[2,13]. This is supported by the fact that no additional procedure related to aortic complications was performed during the mean follow-up of 47.37 months, and no aneurysm-related death occurred.

Conclusions

According to the current literature, the incidence of endograft failure without further options for endovascular salvage keeps rising significantly[6]. Explant results are associated with morbidity and mortality rates that may exceed those found for elective primary repair, due to the technical difficulties that are encountered during LOC and the high surgical risk that characterize this subgroup of patients.

LOC after EVAR with infrarenal clamping of the endograft demonstrated to be a feasible, safe and effective technique, with satisfactory post-operative mortality and morbidity rates. This method, in properly selected patients, allows to simplify the surgical technique, and potentially avoids renal and visceral complications that may be related to a suprarenal or supraceliac clamping.

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Claudio BIANCHINI MASSONI	CB			✔	✔		✔	✔	✔	
Pierfranco SALCUNI	PS	✔				✔	✔	✔		
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