

Abdominal aortic aneurysms: diagnosis and management

Evidence review X: Managing complications after abdominal aortic aneurysm repair

NICE guideline <number>

Evidence review

May 2018

Draft for Consultation

*Commissioned by the National Institute
for Health and Care Excellence*

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the [Welsh Government](#), [Scottish Government](#), and [Northern Ireland Executive](#). All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

© NICE [2018]. All rights reserved. Subject to [Notice of rights](#).

ISBN:

Contents

Managing complications after abdominal aortic aneurysm repair	5
Review question	5
Introduction	5
PICO 5	
Methods and process	5
Clinical evidence	6
Summary of clinical studies included in the evidence review	6
Quality assessment of clinical studies included in the evidence review	6
Economic evidence	6
Evidence statements	7
Recommendations	7
Rationale and impact.....	7
The committee’s discussion of the evidence.....	7
Appendices	10
Appendix A – Review protocols	10
Review protocol for managing post-surgery complications	10
Appendix B – Literature search strategies	12
Clinical search literature search strategy	12
Health Economics literature search strategy	14
Appendix C – Clinical evidence study selection	16
Appendix D – Economic evidence study selection	17
Appendix E – Excluded studies	18
Clinical studies	18
Economic studies	25
Appendix F – Glossary	26

1 Managing complications after abdominal 2 aortic aneurysm repair

3 Review question

4 How should the following complications be managed if they do arise?

- 5 • Endoleak (type II in particular)
- 6 • Expanding aneurysm sac
- 7 • Stent fractures and occlusions
- 8 • Graft infection
- 9 • Graft migration
- 10 • Aortoenteric fistula
- 11 • Aortic rupture
- 12 • Ischaemic complications (limb, visceral and renal)

13 Introduction

14 The aim of this review question was to determine the most effective approach to managing
15 endoleak, expanding aneurysm sac, stent fractures and occlusions, graft infection, graft
16 migration, aortoenteric fistula, aortic rupture, and ischaemic complications (limb, visceral and
17 renal) after abdominal aortic aneurysm (AAA) repair.

18 PICO

19 Table 1: Included studies

Parameter	Inclusion criteria
Population	People who experience a complication (endoleak, expanding aneurysm sac, stent fractures and occlusions, graft infection, graft migration, aortoenteric fistula, aortic rupture, and ischaemic complications (limb, visceral and renal) after undergoing surgical repair of an abdominal aortic aneurysm
Intervention	Open, endovascular or percutaneous surgical intervention
Comparator	Each other, no intervention, sham surgical intervention, or surveillance
Outcomes	Mortality (all-cause; AAA-related; cardiovascular; survival) Adverse events Resolution/recurrence of complication Need for further intervention Quality of life Resource use and cost

20 Methods and process

21 This evidence review was developed using the methods and process described in
22 [Developing NICE guidelines: the manual](#). Methods specific to this review question are
23 described in the review protocol in Appendix A.

24 Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

25 Two literature searches were performed to identify studies assessing the effectiveness of
26 various approaches of managing complications that may arise after EVAR; including,
27 endoleak, expanding aneurysm sac, stent fractures, occlusions, graft infection, graft

28 migration, aortoenteric fistula, aortic rupture, and ischaemic complications. The first literature
29 search used a randomised controlled trial (RCT) and systematic review (SR) filter while the
30 second search used an observational study filter to identify potentially relevant studies. The
31 databases were sifted to identify all studies that met the criteria detailed in Table 1. The full
32 review protocol can be found in Appendix A.

33 The reviewer sifted the RCT database to identify evidence from RCTs, quasi-randomised
34 controlled trials and systematic reviews of the aforementioned study designs that met the
35 inclusion criteria. If limited evidence was identified, the observational study database was
36 sifted to identify non-randomised controlled trials and prospective cohort studies recruiting a
37 population of 500 or more people who had one of the complications of interest.

38 Studies were excluded if they were:

- 39 • Case-control or cross-sectional studies
- 40 • Not in English
- 41 • Not full reports of the study (for example, published only as an abstract)
- 42 • Not peer-reviewed.

43 **Clinical evidence**

44 **Included studies**

45 The database from initial literature searches provided 3,697 abstracts, and an additional 7
46 papers were identified through citation searching of studies screened at full-text. Of these
47 3,704 citations, 84 were identified as being potentially relevant. Following full-text review of
48 these articles, 0 studies were found that met the criteria outlined in the protocol.

49 An update search was conducted in December 2017, to identify any relevant studies
50 published during guideline development. The search yielded 125 abstracts; all of which were
51 not considered relevant to this review question. As a result no additional studies were
52 identified.

53 **Excluded studies**

54 For the list of studies excluded at full-text, with details, see Appendix E.

55 **Summary of clinical studies included in the evidence review**

56 No studies were included following full text review.

57 **Quality assessment of clinical studies included in the evidence review**

58 No studies were included following full text review.

59 **Economic evidence**

60 **Included studies**

61 An initial literature search was conducted jointly for all review questions by applying standard
62 health economic filters to a clinical search for AAA. This search returned a total of 5,173
63 citations. Following review of all titles and abstracts, no studies were identified as being
64 potentially relevant to the review question. No full texts were retrieved, and no studies were
65 included as economic evidence.

66 An update search was conducted in December 2017, to identify any relevant health
67 economic analyses published during guideline development. The search yielded 814

68 abstracts; all of which were not considered relevant to this review question. As a result no
69 additional studies were identified.

70 **Excluded studies**

71 No studies were retrieved for full-text review.

72 **Evidence statements**

73 No evidence was identified for this review question.

74 **Recommendations**

75 X1. Consider open, endovascular or percutaneous intervention for type I and type III
76 endoleaks following EVAR.

77 X2. Consider intervention for type II endoleaks in people who have sac expansion following
78 EVAR.

79 X3. Consider further investigation of type V endoleak following EVAR.

80 **Rationale and impact**

81 **Why the committee made the recommendations**

82 Endoleak following EVAR is common, and can have a negative impact on patient prognosis
83 and long-term quality of life. In the absence of evidence, the committee made
84 recommendations based on their experience because:

- 85 • it is good practice to repair type I and III endoleaks and some type II endoleaks
- 86 • healthcare professionals are not all aware that type II endoleaks without sac expansion
87 can be managed conservatively
- 88 • there are circumstances when sac expansion occurs without imaging evidence of a leak
89 site (called type V endoleak), and these situations need further investigation.

90 **Impact of the recommendations on practice**

91 The recommendations will have minimal impact on current practice as it is common practice
92 to intervene for type I and type III endoleaks, and type II endoleaks if there is evidence of
93 aneurysm sac expansion.

94 **The committee's discussion of the evidence**

95 **Interpreting the evidence**

96 ***The outcomes that matter most***

97 The committee agreed that the outcomes that matter most are the persistence or recurrence
98 of endoleaks, AAA sac expansion and rupture which in turn poses a risk of mortality.

99 ***The quality of the evidence***

100 No RCTs, quasi-randomised controlled trials or cohort studies with sample sizes of 500 or
101 more were found. The committee discussed the potential usefulness of gathering evidence
102 from small retrospective cohort studies and case series but agreed that none of these types
103 of studies would have sufficient quality, or statistical power, to be useful for their decision
104 making.

105 **Benefits and harms**

106 The committee noted that endoleaks pose a risk of sac expansion and rupture, and agreed
107 that there are a variety of open, endovascular and percutaneous surgical interventions that
108 can be used to resolve them. This in turn can prevent long-term complications that can have
109 a negative impact on quality of life. They noted that endoleaks almost exclusively occur
110 following EVAR as opposed to open repair, and therefore the informal consensus
111 recommendations should be focused on people who have undergone surgical intervention
112 via EVAR.

113 The committee agreed that, based on their clinical experience, type II endoleak, the most
114 common form of post-EVAR endoleak, may be considered benign if found in the absence of
115 signs of sac expansion. As such, a recommendation to consider intervention for type II
116 endoleaks only in people who have sac expansion following EVAR discourages interventions
117 that, in the absence of sac expansion, may be more harmful than beneficial.

118 The committee noted that it is common practice to intervene for the majority of type I and III
119 endoleaks. However, the committee advised that for all endoleaks, even type I and III, there
120 are instances in which practitioners would not intervene. The committee therefore agreed
121 that a recommendation to 'offer' interventions for type I-III endoleaks should not be made,
122 due to a lack of evidence and due to instances existing in which intervention for endoleaks
123 would be inappropriate for the affected person.

124 The committee noted that type IV endoleaks can occur after some EVAR procedures, due to
125 the porosity of certain graft materials, but usually resolve on their own without the need for
126 intervention. As a result, it was agreed that no recommendations were needed in relation to
127 type IV endoleaks.

128 The committee noted that a type V endoleak (also referred to as endotension) is a
129 phenomenon in which there is continued sac expansion without imaging evidence of a leak
130 site. Due to the risk of mortality associated with aneurysm sac expansion, the committee
131 agreed that it would be appropriate to consider further investigations to identify the cause of
132 sac expansion, and to see if the underlying cause is one that may be treatable.

133 The committee identified several risks of endoleak intervention but agreed that these were
134 too small in magnitude and/or frequency to influence recommendations. These included
135 small risks of procedural harm and the potential for over-treating and/or over-investigating
136 people, particularly in those with difficult-to-treat endoleaks. There is also a small risk of
137 radiation-induced malignancy associated with repeated exposure to ionising radiation during
138 CT imaging. However, this risk was agreed to be small, because the average life expectancy
139 following EVAR is too short for radiation-induced cancer to develop in most people
140 undergoing endoleak surveillance or intervention.

141 For the other complications specified in this review (stent fractures and occlusions, graft
142 infection, graft migration, aortoenteric fistula, secondary aortic rupture and ischaemic
143 complications), the committee agreed it was neither possible nor useful to give consensus
144 recommendations on how they should be managed. This was because there is established
145 practice for their management, or a general lack of consensus as to best practice for
146 management.

147 **Cost effectiveness and resource use**

148 The committee agreed that the recommendations are unlikely to impact on costs and
149 resource use. This is because interventions for endoleaks and investigations for causes of
150 aneurysm sac expansion are already performed in practice, and the recommendations
151 reinforce their importance. The committee also noted that the costs associated with treating
152 endoleaks would be offset by savings arising from the prevention of long-term complications
153 associated with endoleak.

154 **Other considerations**

155 The committee agreed that there was no reason to believe that management of
156 complications should be different between women and men, and therefore considered that
157 the recommendations would apply to all people who have undergone EVAR.

158 Studies relating to the EUROSTAR registry were reviewed for inclusion. However, these
159 assessed primarily incidence and prognosis of post-repair complications and none compared
160 the efficacy of surgical interventions in the management of these complications.

161

1 Appendices

2 Appendix A – Review protocols

Review protocol for managing post-surgery complications

Review question 31	How should the following complications be managed if they do arise? <ul style="list-style-type: none"> • Endoleak (type II in particular) • Expanding aneurysm sac • Stent fractures and occlusions • Graft infection • Graft migration • Aortoenteric fistula • Aortic rupture • Ischaemic complications (limb, visceral and renal)
Objectives	To determine the most effective approach to managing endoleak, expanding aneurysm sac, stent fractures and occlusions, graft infection, graft migration, aortoenteric fistula, aortic rupture, and ischaemic complications (limb, visceral and renal)
Type of review	Intervention
Language	English only
Study design	Systematic reviews of study designs listed below <ul style="list-style-type: none"> • Randomised controlled trials • Quasi-randomised controlled trials If insufficient evidence identified, non-randomised controlled trials and prospective cohort studies (n >500 if not specifically recruiting a population with a complication of interest)
Status	Published papers only (full text) No date restrictions
Population	People who experience a complication (endoleak, expanding aneurysm sac, stent fractures and occlusions, graft infection, graft migration, aortoenteric fistula, aortic rupture, and ischaemic complications (limb, visceral and renal) after undergoing surgical repair of an AAA
Intervention	Open, endovascular or percutaneous surgical intervention
Comparator	Each other, no intervention, sham surgical intervention, or surveillance
Outcomes	<ul style="list-style-type: none"> • Mortality (all-cause; AAA-related; cardiovascular; survival) • Adverse events • Resolution/recurrence of complication • Need for further intervention • Quality of life • Resource use and cost
Other criteria for inclusion / exclusion of studies	Exclusion: <ul style="list-style-type: none"> • Non-English language • Abstract/non-published

Review question 31	How should the following complications be managed if they do arise? <ul style="list-style-type: none"> • Endoleak (type II in particular) • Expanding aneurysm sac • Stent fractures and occlusions • Graft infection • Graft migration • Aortoenteric fistula • Aortic rupture • Ischaemic complications (limb, visceral and renal)
Baseline characteristics to be extracted in evidence tables	<ul style="list-style-type: none"> • Age • Sex • Size of aneurysm • Comorbidities
Search strategies	See Appendix B
Review strategies	<p>Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies.</p> <p>Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect.</p> <p>All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.</p>
Key papers	https://icvts.oxfordjournals.org/content/20/1/128.full.pdf https://www.ncbi.nlm.nih.gov/pubmed/23939840

1

Appendix B – Literature search strategies

Clinical search literature search strategy

Main searches

- 4 Bibliographic databases searched for the guideline
- 5 • Cumulative Index to Nursing and Allied Health Literature - CINAHL (EBSCO)
- 6 • Cochrane Database of Systematic Reviews – CDSR (Wiley)
- 7 • Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- 8 • Database of Abstracts of Reviews of Effects – DARE (Wiley)
- 9 • Health Technology Assessment Database – HTA (Wiley)
- 10 • EMBASE (Ovid)
- 11 • MEDLINE (Ovid)
- 12 • MEDLINE Epub Ahead of Print (Ovid)
- 13 • MEDLINE In-Process (Ovid)

Identification of evidence for review questions

15 The searches were conducted between November 2015 and October 2017 for 31 review
16 questions (RQ). In collaboration with Cochrane, the evidence for several review questions
17 was identified by an update of an existing Cochrane review. Review questions in this
18 category are indicated below. Where review questions had a broader scope, supplement
19 searches were undertaken by NICE.

20 Searches were re-run in December 2017.

21 Where appropriate, study design filters (either designed in-house or by McMaster) were used
22 to limit the retrieval to, for example, randomised controlled trials. Details of the study design
23 filters used can be found in section 4.

Search strategy review question 31

Medline Strategy, searched 18th October 2017

Database: Ovid MEDLINE(R) 1946 to October Week 1 2017

Search Strategy:

- 1 Aortic Aneurysm, Abdominal/ (18071)
- 2 (aneurysm* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort* or spontan* or
juxtarenal* or juxta-renal* or juxta renal* or paraarenal* or para-renal* or para renal* or suprarenal*
or supra renal* or supra-renal* or short neck* or short-neck* or shortneck* or visceral aortic
segment*).tw. (36093)
- 3 AAA*.tw. (13513)
- 4 or/1-3 (45989)
- 5 exp Perioperative Care/ (149869)
- 6 (postsurg* or post-surg* or post surg* or postop* or post-op* or post op* or post-endovascular*
or post endovascular* or post endovascular*).tw. (513005)
- 7 ((after or following or followed or electiv* or post*) adj4 (surg* or operat* or procedure* or
repair* or care* or outcome*).tw. (714418)
- 8 or/5-7 (1062271)
- 9 Elective Surgical Procedures/ (12513)
- 10 Endovascular Procedures/ or Vascular Surgical Procedures/ (42604)

Medline Strategy, searched 18th October 2017

Database: Ovid MEDLINE(R) 1946 to October Week 1 2017

Search Strategy:

- 11 (endovascular* adj4 aneurysm* adj4 repair*).tw. (4258)
- 12 (endovascular adj4 aort* adj4 repair*).tw. (4633)
- 13 (upper adj4 abdominal adj4 (repair* or surger* or surgic* or operat* or procedur*)).tw.
- 14 (EVAR or EVRAR or FEVAR or F-EAVAR or BEVAR or B-EVAR).tw.
- 15 (Anaconda or Zenith Dynalink or Hemobahn or Luminex* or Memoth-erm or Wallstent).tw.
- 16 (Viabahn or Nitinol or Hemobahn or Intracoil or Tantalum).tw.
- 17 or/9-16
- 18 4 and 8 and 17
- 19 Aortic Aneurysm, Abdominal/su [Surgery]
- 20 8 and 19
- 21 18 or 20
- 22 (manag* adj4 complication*).tw.
- 23 Endoleak/
- 24 Prosthesis Failure/
- 25 (endoleak or (perigraft* adj4 leak*)).tw.
- 26 (prosthe* adj4 (fail* or loose* or migrat* or break* or fail*)).tw.
- 27 Postoperative Hemorrhage/
- 28 (haemorrhag* or hemorrhag* or bleed* or blood-loss or bloodloss or blood loss).tw.
- 29 (blood adj4 los*).tw.
- 30 (expan* adj4 aneurysm* adj4 sac*).tw.
- 31 (expan* adj4 AAA adj4 sac*).tw.
- 32 (rupture* adj4 sac*).tw.
- 33 Stents/ae [Adverse Effects]
- 34 (stent* adj4 (fractur* or occlus*)).tw.
- 35 Prosthesis-Related Infections/
- 36 ((prosthe* or graft* or endograft*) adj4 infect*).tw.
- 37 ((graft* or endograft*) adj4 (fail* or loose* or migrat* or break* or fail*)).tw.
- 38 Intestinal Fistula/
- 39 ((intestin* or cholecystoduoden* or colovesic* or enterocutan* or aortoenteric* or bowel* or enteric*) adj4 fistul*).tw.
- 40 (aliment* adj4 tract* adj4 fistul*).tw.
- 41 Aortic Rupture/
- 42 RAAA.tw.
- 43 ((aort* or aneurysm*) adj4 ruptur*).tw.
- 44 Ischemia/
- 45 ((limb* or lower-limb* or visceral* or intestin* or colon* or bowel* or mesenteric* or renal* or kidney* or nephric* or asnephric*) adj4 (ischaemi* or ischemi*)).tw.
- 46 (blood adj4 deficien* adj4 (limb* or lower-limb* or visceral* or intestin* or colon* or bowel* or mesenteric* or renal* or kidney* or nephric* or asnephric*)).tw.
- 47 (insufficien* adj4 blood adj4 (limb* or lower-limb* or visceral* or intestin* or colon* or bowel* or mesenteric* or renal* or kidney* or nephric* or asnephric*)).tw.
- 48 (decreas* adj4 blood adj4 (limb* or lower-limb* or visceral* or intestin* or colon* or bowel* or mesenteric* or renal* or kidney* or nephric* or asnephric*)).tw.
- 49 (reduc* adj4 blood adj4 (limb* or lower-limb* or visceral* or intestin* or colon* or bowel* or mesenteric* or renal* or kidney* or nephric* or asnephric*)).tw.
- 50 (circulat* adj4 (disorder* or fail* or disturb*) adj4 (limb* or lower-limb* or visceral* or intestin* or colon* or bowel* or mesenteric* or renal* or kidney* or nephric* or asnephric*)).tw.
- 51 or/22-50
- 52 21 and 51

Medline Strategy, searched 18th October 2017
Database: Ovid MEDLINE(R) 1946 to October Week 1 2017
Search Strategy:

53 animals/ not humans/
54 52 not 53
55 limit 54 to english language

Health Economics literature search strategy

Sources searched to identify economic evaluations

- 3 • NHS Economic Evaluation Database – NHS EED (Wiley) last updated Dec 2014
 - 4 • Health Technology Assessment Database – HTA (Wiley) last updated Oct 2016
 - 5 • Embase (Ovid)
 - 6 • MEDLINE (Ovid)
 - 7 • MEDLINE In-Process (Ovid)
- 8 Search filters to retrieve economic evaluations and quality of life papers were appended to
9 the population and intervention terms to identify relevant evidence. Searches were not
10 undertaken for qualitative RQs. For social care topic questions additional terms were added.
11 Searches were re-run in September 2017 where the filters were added to the population
12 terms.

Health economics search strategy

Medline Strategy

Economic evaluations

- 1 Economics/
- 2 exp "Costs and Cost Analysis"/
- 3 Economics, Dental/
- 4 exp Economics, Hospital/
- 5 exp Economics, Medical/
- 6 Economics, Nursing/
- 7 Economics, Pharmaceutical/
- 8 Budgets/
- 9 exp Models, Economic/
- 10 Markov Chains/
- 11 Monte Carlo Method/
- 12 Decision Trees/
- 13 econom*.tw.
- 14 cba.tw.
- 15 cea.tw.
- 16 cua.tw.
- 17 markov*.tw.
- 18 (monte adj carlo).tw.
- 19 (decision adj3 (tree* or analys*)).tw.
- 20 (cost or costs or costing* or costly or costed).tw.
- 21 (price* or pricing*).tw.
- 22 budget*.tw.
- 23 expenditure*.tw.
- 24 (value adj3 (money or monetary)).tw.

Medline Strategy

25 (pharmacoeconomic* or (pharmaco adj economic*)).tw.
26 or/1-25

Quality of life

1 "Quality of Life"/
2 quality of life.tw.
3 "Value of Life"/
4 Quality-Adjusted Life Years/
5 quality adjusted life.tw.
6 (qaly* or qald* or qale* or qtime*).tw.
7 disability adjusted life.tw.
8 daly*.tw.
9 Health Status Indicators/
10 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
11 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
12 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
13 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
14 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
15 (euroqol or euro qol or eq5d or eq 5d).tw.
16 (qol or hql or hqol or hrqol).tw.
17 (hye or hyes).tw.
18 health* year* equivalent*.tw.
19 utilit*.tw.
20 (hui or hui1 or hui2 or hui3).tw.
21 disutili*.tw.
22 rosser.tw.
23 quality of wellbeing.tw.
24 quality of well-being.tw.
25 qwb.tw.
26 willingness to pay.tw.
27 standard gamble*.tw.
28 time trade off.tw.
29 time tradeoff.tw.
30 tto.tw.
31 or/1-30

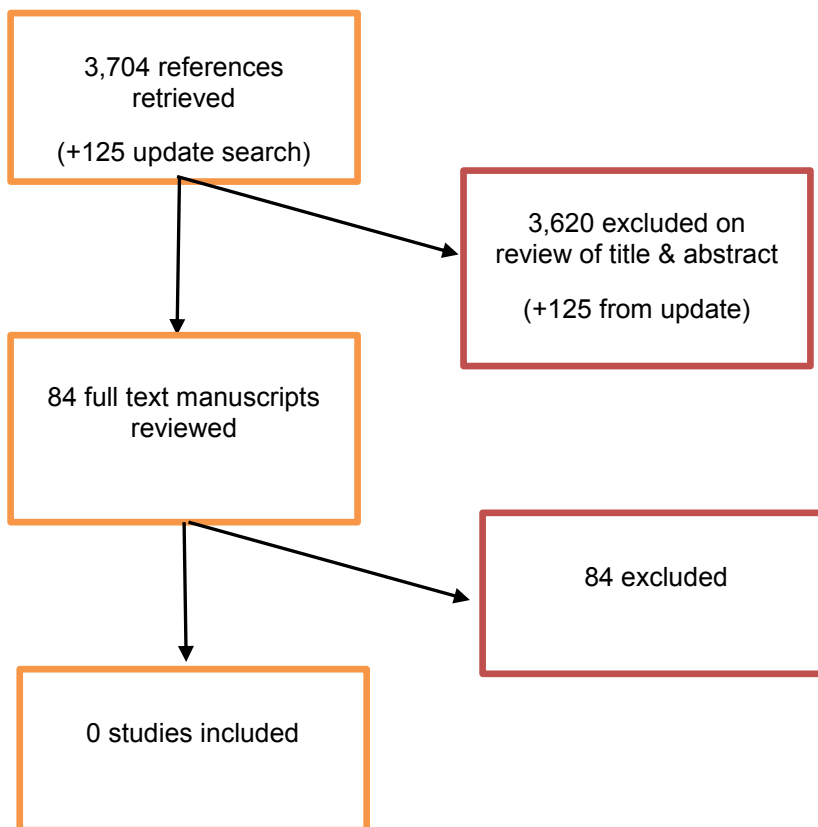
1

Appendix C – Clinical evidence study selection

2

3

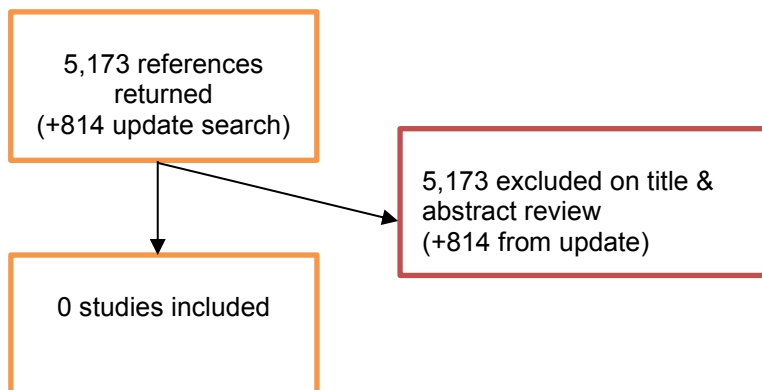
4



Appendix D – Economic evidence study selection

2

3



Appendix E – Excluded studies

Clinical studies

Short Title	Title	Reason for exclusion
AbuRahma (2017)	Management of Immediate Post-Endovascular Aortic Aneurysm Repair Type Ia Endoleaks and Late Outcomes	Full text screen • Study does not contain a relevant comparison or population
Alvarez (2017)	Effect of antiplatelet therapy on aneurysmal sac expansion associated with type II endoleaks after endovascular aneurysm repair	Full text screen • Study does not contain a relevant comparison or population
Ammar (2016)	Comparative effect of propofol versus sevoflurane on renal ischemia/reperfusion injury after elective open abdominal aortic aneurysm repair	Full text screen • Study does not contain a surgical intervention
Argyriou (2017)	Endograft Infection After Endovascular Abdominal Aortic Aneurysm Repair: A Systematic Review and Meta-analysis	Full text screen • Review paper where all relevant primary studies have been included separately
Baril (2008)	Endovascular stent-graft repair of failed endovascular abdominal aortic aneurysm repair	Full text screen • Retrospective study with a sample size less than 500 participants
Bastos (2014)	Spontaneous delayed sealing in selected patients with a primary type-Ia endoleak after endovascular aneurysm repair	Full text screen • Study does not contain a relevant comparison or population
Baum (2002)	Treatment of type II endoleaks after endovascular repair of abdominal aortic aneurysms: comparison of transarterial and translumbar techniques	Full text screen • Retrospective study with a sample size less than 500 participants
Burks (2001)	Endovascular repair of bleeding aortoenteric fistulas: a 5-year experience	Full text screen • Case report or too few participants in one or more arms
Capoccia (2016)	Preliminary Results from a National Enquiry of Infection in Abdominal Aortic Endovascular Repair (Registry of Infection in EVAR--R.I.EVAR).	Full text screen • Retrospective study with a sample size less than 500 participants
Choi (2011)	Treatment of type I endoleaks after endovascular aneurysm repair of infrarenal abdominal aortic aneurysm: usefulness of N-butyl cyanoacrylate embolization in cases of failed secondary endovascular intervention	Full text screen • Study does not contain a relevant comparison or population

Short Title	Title	Reason for exclusion
Darling (1999)	The incidence, natural history, and outcome of secondary intervention for persistent collateral flow in the excluded abdominal aortic aneurysm	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Davila (2015)	A multicenter experience with the surgical treatment of infected abdominal aortic endografts	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Donas (2015)	Use of parallel grafts to save failed prior endovascular aortic aneurysm repair and type Ia endoleaks	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Eli (2016)	Long-term outcomes of embolization of type II endoleaks	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Faries (2003)	Management of endoleak after endovascular aneurysm repair: cuffs, coils, and conversion	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Ferrero (2013)	Open conversion after endovascular aortic aneurysm repair: a single-center experience	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Fichelle (1993)	Infected infrarenal aortic aneurysms: when is in situ reconstruction safe?	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Freischlag (2002)	Treatment of type 2 endoleaks after endovascular repair of abdominal aortic aneurysms: Comparison of transarterial and translumbar techniques: Discussion	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Gandini (2014)	Treatment of type II endoleak after endovascular aneurysm repair: the role of selective vs. nonselective transcaval embolization	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Gallagher (2012)	Midterm outcomes after treatment of type II endoleaks associated with aneurysm sac expansion	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Gelfand (2006)	Clinical significance of type II endoleak after endovascular repair of abdominal aortic aneurysm	Full text screen <ul style="list-style-type: none"> • Review paper where all relevant primary studies have been included separately
Gorich (2000)	Treatment of leaks after endovascular repair of aortic aneurysms	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Case report or too few participants in one or more arms
Hajibandeh (2015)	Is intervention better than surveillance in patients with type 2 endoleak post-	Full text screen <ul style="list-style-type: none"> • Review paper where all relevant primary

Short Title	Title	Reason for exclusion
	endovascular abdominal aortic aneurysm repair?	studies have been included separately
Halak (2007)	Open surgical treatment of aneurysmal sac expansion following endovascular abdominal aneurysm repair: solution for an unresolved clinical dilemma	Full text screen <ul style="list-style-type: none"> • Case report or too few participants in one or more arms
Jim (2011)	Midterm outcomes of the Zenith Renu AAA Ancillary Graft	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Jones (2007)	Persistent type 2 endoleak after endovascular repair of abdominal aortic aneurysm is associated with adverse late outcomes	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Study does not provide any/sufficient outcome data of interest
Jouhannet (2014)	Reinterventions for type 2 endoleaks with enlargement of the aneurysmal sac after endovascular treatment of abdominal aortic aneurysms	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Kakkos (2011)	Open or endovascular repair of aortoenteric fistulas? A multicentre comparative study	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Karthikesalingam (2012)	Current evidence is insufficient to define an optimal threshold for intervention in isolated type II endoleak after endovascular aneurysm repair.	Full text screen <ul style="list-style-type: none"> • Review paper where all relevant primary studies have been included separately
Katsargyris (2013)	Fenestrated stent-grafts for salvage of prior endovascular abdominal aortic aneurysm repair	Full text screen <ul style="list-style-type: none"> • Case report or too few participants in one or more arms
Khaja (2014)	Treatment of type II endoleak using Onyx with long-term imaging follow-up	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
La Barbera (2003)	Aorto-caval fistula: A complication of ruptured abdominal aortic aneurysms	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Case report or too few participants in one or more arms • Study does not provide any/sufficient outcome data of interest
Laser (2011)	Graft infection after endovascular abdominal aortic aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Law (2016)	Effectiveness of proximal intra-operative salvage Palmaz stent placement for endoleak during endovascular aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population

Short Title	Title	Reason for exclusion
Leurs (2007)	Secondary interventions after elective endovascular repair of degenerative thoracic aortic aneurysms: results of the European collaborators registry (EUROSTAR)	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Lindblad (2008)	What to do when evidence is lacking - Implications on treatment of aortic ulcers, pseudoaneurysms and aorto-enteric fistulae	Full text screen <ul style="list-style-type: none"> • Case report or too few participants in one or more arms
Lynch (2004)	Clinical outcome and factors predictive of recurrence after enterocutaneous fistula surgery	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Maitrias (2016)	Treatment of sac expansion after endovascular aneurysm repair with obliterating endoaneurysmorrhaphy and stent graft preservation	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Maldonado (2004)	Ischemic complications after endovascular abdominal aortic aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Maleux (2001)	Late distal perigraft endoleak after endovascular repair of an abdominal aortic aneurysm due to cranial migration of the iliac branch of a modular stent-graft	Full text screen <ul style="list-style-type: none"> • Case report or too few participants in one or more arms
Maleux (2017)	Incidence, etiology, and management of type III endoleak after endovascular aortic repair	Full text screen <ul style="list-style-type: none"> • Study does not provide any/sufficient outcome data of interest
Marcelin (2017)	Safety and efficacy of embolization using Onyx of persistent type II endoleaks after abdominal endovascular aneurysm repair	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Massis (2012)	Treatment of type II endoleaks with ethylene-vinyl-alcohol copolymer (Onyx).	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Maze (2013)	Outcomes of infected abdominal aortic grafts managed with antimicrobial therapy and graft retention in an unselected cohort	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Moulakakis (2017)	Treatment of Type II Endoleak and Aneurysm Expansion after EVAR	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Nevala (2010)	Type II endoleak after endovascular repair of abdominal aortic aneurysm: effectiveness of embolization	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants

Short Title	Title	Reason for exclusion
Ogawa (2016)	A multi-institutional survey of interventional radiology for type II endoleaks after endovascular aortic repair: questionnaire results from the Japanese Society of Endoluminal Metallic Stents and Grafts in Japan	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Ozdemir (2013)	Embolisation of type 2 endoleaks after endovascular aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Patatas (2012)	Static sac size with a type II endoleak post-endovascular abdominal aortic aneurysm repair: surveillance or embolization?	Full text screen <ul style="list-style-type: none"> • Non-systematic review
Pettersson (2017)	Aortic Graft Infections after Emergency and Non-Emergency Reconstruction: incidence, Treatment, and Long-Term Outcome	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population Pools TAA, AAA AIOD patients
Piffaretti (2017)	Operative Treatment of Type II Endoleaks Involving the Inferior Mesenteric Artery	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Pitoulis (2009)	Secondary endovascular and conversion procedures for failed endovascular abdominal aortic aneurysm repair: can we still be optimistic?	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Prokakis (2008)	Aorto-esophageal fistulas due to thoracic aorta aneurysm: surgical versus endovascular repair. Is there a role for combined aortic management?	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Ricotta (2010)	Endoleak management and postoperative surveillance following endovascular repair of thoracic aortic aneurysms	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Non-systematic review
Saito (2012)	Outcome of surgical repair of aorto-esophageal fistulas with cryopreserved aortic allografts	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Sampram (2003)	Nature, frequency, and predictors of secondary procedures after endovascular repair of abdominal aortic aneurysm	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Sarac (2012)	Long-term follow-up of type II endoleak embolization reveals the need for close surveillance	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Scali (2014)	Elective endovascular aortic repair conversion for type Ia endoleak is not associated	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant

Short Title	Title	Reason for exclusion
	with increased morbidity or mortality compared with primary juxtarenal aneurysm repair	comparison or population
Schmieder (2009)	Endoleak after endovascular aneurysm repair: duplex ultrasound imaging is better than computed tomography at determining the need for intervention	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Schoell (2015)	Surgery for secondary aorto-enteric fistula or erosion (SAEFE) complicating aortic graft replacement: a retrospective analysis of 32 patients with particular focus on digestive management	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Seeger (2000)	Long-term outcome after treatment of aortic graft infection with staged extra-anatomic bypass grafting and aortic graft removal	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Sharif (2007)	Prosthetic stent graft infection after endovascular abdominal aortic aneurysm repair	Full text screen <ul style="list-style-type: none"> • Case report or too few participants in one or more arms
Sheehan (2004)	Effectiveness of coiling in the treatment of endoleaks after endovascular repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Sheehan (2006)	Are type II endoleaks after endovascular aneurysm repair endograft dependent?	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Sidloff (2013)	Type II endoleak after endovascular aneurysm repair	Full text screen <ul style="list-style-type: none"> • Review paper where all relevant primary studies have been included separately
Skibba (2015)	Management of late main-body aortic endograft component uncoupling and type IIIa endoleak encountered with the Endologix Powerlink and AFX platforms	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Study does not contain a surgical intervention
Smeds (2016)	Treatment and outcomes of aortic endograft infection.	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Spanos (2016)	Systematic review and meta-analysis of migration after endovascular abdominal aortic aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Spanos (2017)	Laparoscopic ligation of inferior mesenteric artery for the treatment of type II	Full text screen <ul style="list-style-type: none"> • Review paper where all relevant primary studies have been included separately

Short Title	Title	Reason for exclusion
	endoleak after endovascular aortic aneurysm repair	
Steinmetz (2004)	Type II endoleak after endovascular abdominal aortic aneurysm repair: A conservative approach with selective intervention is safe and cost-effective	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Thomas (2010)	A comparative analysis of the outcomes of aortic cuffs and converters for endovascular graft migration	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
Tolia (2005)	Type II endoleaks after endovascular repair of abdominal aortic aneurysms: natural history	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Tzortzis (2003)	Adjunctive procedures for the treatment of proximal type I endoleak: the role of peri-aortic ligatures and Palmaz stenting	Full text screen <ul style="list-style-type: none"> • Paper not available
Uthoff (2012)	Direct percutaneous sac injection for postoperative endoleak treatment after endovascular aortic aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Study does not contain a surgical intervention • Case report or too few participants in one or more arms
Vaislic (2016)	Three-Year Outcomes with the Multilayer Flow Modulator for Repair of Thoracoabdominal Aneurysms: a Follow-up Report from the STRATO Trial	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Vaislic (2017)	Four-year outcomes with the multilayer flow modulator for repair of thoracoabdominal aneurysms: a follow-up report from the STRATO trial	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Valentine (1998)	Gastrointestinal complications after aortic surgery	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Case report or too few participants in one or more arms
van Lammeren (2010)	Long-term follow-up of secondary interventions after endovascular aneurysm repair with the AneuRx endoprosthesis: a single-center experience	Full text screen <ul style="list-style-type: none"> • Retrospective study with a sample size less than 500 participants
van Zeggeren (2013)	Incidence and treatment results of Endurant endograft occlusion	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population

Short Title	Title	Reason for exclusion
Velazquez (2000)	Relationship between preoperative patency of the inferior mesenteric artery and subsequent occurrence of type II endoleak in patients undergoing endovascular repair of abdominal aortic aneurysms	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Vogt (1998)	Cryopreserved arterial allografts in the treatment of major vascular infection: a comparison with conventional surgical techniques	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Walker (2015)	Type II endoleak with or without intervention after endovascular aortic aneurysm repair does not change aneurysm-related outcomes despite sac growth	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population
Wang (2017)	Limb graft occlusion following endovascular aortic repair: Incidence, causes, treatment and prevention in a study cohort	Full text screen <ul style="list-style-type: none"> • Case report or too few participants in one or more arms
Zacharias (2016)	Anatomic characteristics of abdominal aortic aneurysms presenting with delayed rupture after endovascular aneurysm repair	Full text screen <ul style="list-style-type: none"> • Study does not contain a relevant comparison or population • Study does not contain a surgical intervention

Economic studies

2 No full text papers were retrieved. All studies were excluded at review of titles and abstracts.

3

Appendix F – Glossary

1Abdominal Aortic Aneurysm (AAA)

3 A localised bulge in the abdominal aorta (the major blood vessel that supplies blood to the
4 lower half of the body including the abdomen, pelvis and lower limbs) caused by weakening
5 of the aortic wall. It is defined as an aortic diameter greater than 3 cm or a diameter more
6 than 50% larger than the normal width of a healthy aorta. The clinical relevance of AAA is
7 that the condition may lead to a life threatening rupture of the affected artery. Abdominal
8 aortic aneurysms are generally characterised by their shape, size and cause:

- 9 • Infrarenal AAA: an aneurysm located in the lower segment of the abdominal aorta
10 below the kidneys.
- 11 • Juxtarenal AAA: a type of infrarenal aneurysm that extends to, and sometimes,
12 includes the lower margin of renal artery origins.
- 13 • Suprarenal AAA: an aneurysm involving the aorta below the diaphragm and above
14 the renal arteries involving some or all of the visceral aortic segment and hence the
15 origins of the renal, superior mesenteric, and celiac arteries, it may extend down to
16 the aortic bifurcation.

1Abdominal compartment syndrome

18 Abdominal compartment syndrome occurs when the pressure within the abdominal cavity
19 increases above 20 mm Hg (intra-abdominal hypertension). In the context of a ruptured AAA
20 this is due to the mass effect of a volume of blood within or behind the abdominal cavity. The
21 increased abdominal pressure reduces blood flow to abdominal organs and impairs
22 pulmonary, cardiovascular, renal, and gastro-intestinal function. This can cause multiple
23 organ dysfunction and eventually lead to death.

2Cardiopulmonary exercise testing

25 Cardiopulmonary Exercise Testing (CPET, sometimes also called CPX testing) is a non-
26 invasive approach used to assess how the body performs before and during exercise. During
27 CPET, the patient performs exercise on a stationary bicycle while breathing through a
28 mouthpiece. Each breath is measured to assess the performance of the lungs and
29 cardiovascular system. A heart tracing device (Electrocardiogram) will also record the hearts
30 electrical activity before, during and after exercise.

3Device migration

32 Migration can occur after device implantation when there is any movement or displacement
33 of a stent-graft from its original position relative to the aorta or renal arteries. The risk of
34 migration increases with time and can result in the loss of device fixation. Device migration
35 may not need further treatment but should be monitored as it can lead to complications such
36 as aneurysm rupture or endoleak.

37

Endoleak

2 An endoleak is the persistence of blood flow outside an endovascular stent - graft but within
3 the aneurysm sac in which the graft is placed.

- 4 • Type I – Perigraft (at the proximal or distal seal zones): This form of endoleak is
5 caused by blood flowing into the aneurysm because of an incomplete or ineffective
6 seal at either end of an endograft. The blood flow creates pressure within the sac and
7 significantly increases the risk of sac enlargement and rupture. As a result, Type I
8 endoleaks typically require urgent attention.
- 9 • Type II – Retrograde or collateral (mesenteric, lumbar, renal accessory): These
10 endoleaks are the most common type of endoleak. They occur when blood bleeds
11 into the sac from small side branches of the aorta. They are generally considered
12 benign because they are usually at low pressure and tend to resolve spontaneously
13 over time without any need for intervention. Treatment of the endoleak is indicated if
14 the aneurysm sac continues to expand.
- 15 • Type III – Midgraft (fabric tear, graft dislocation, graft disintegration): These
16 endoleaks occur when blood flows into the aneurysm sac through defects in the
17 endograft (such as graft fractures, misaligned graft joints and holes in the graft fabric).
18 Similarly to Type I endoleak, a Type III endoleak results in systemic blood pressure
19 within the aneurysm sac that increases the risk of rupture. Therefore, Type III
20 endoleaks typically require urgent attention.
- 21 • Type IV– Graft porosity: These endoleaks often occur soon after AAA repair and are
22 associated with the porosity of certain graft materials. They are caused by blood
23 flowing through the graft fabric into the aneurysm sac. They do not usually require
24 treatment and tend to resolve within a few days of graft placement.
- 25 • Type V – Endotension: A Type V endoleak is a phenomenon in which there is
26 continued sac expansion without radiographic evidence of a leak site. It is a poorly
27 understood abnormality. One theory that it is caused by pulsation of the graft wall,
28 with transmission of the pulse wave through the aneurysm sac to the native
29 aneurysm wall. Alternatively it may be due to intermittent leaks which are not
30 apparent at imaging. It can be difficult to identify and treat any cause.

3 Endovascular aneurysm repair

32 Endovascular aneurysm repair (EVAR) is a technique that involves placing a stent –graft
33 prosthesis within an aneurysm. The stent-graft is inserted through a small incision in the
34 femoral artery in the groin, then delivered to the site of the aneurysm using catheters and
35 guidewires and placed in position under X-ray guidance.

- 36 • Conventional EVAR refers to placement of an endovascular stent graft in an AAA
37 where the anatomy of the aneurysm is such that the ‘instructions for use’ of that
38 particular device are adhered to. Instructions for use define tolerances for AAA
39 anatomy that the device manufacturer considers appropriate for that device. Common
40 limitations on AAA anatomy are infrarenal neck length (usually >10mm), diameter
41 (usually ≤30mm) and neck angle relative to the main body of the AAA
- 42 • Complex EVAR refers to a number of endovascular strategies that have been
43 developed to address the challenges of aortic proximal neck fixation associated with
44 complicated aneurysm anatomies like those seen in juxtarenal and suprarenal AAAs.
45 These strategies include using conventional infrarenal aortic stent grafts outside their
46 ‘instructions for use’, using physician-modified endografts, utilisation of customised

1 fenestrated endografts, and employing snorkel or chimney approaches with parallel
2 covered stents.

Goal directed therapy

4 Goal directed therapy refers to a method of fluid administration that relies on minimally
5 invasive cardiac output monitoring to tailor fluid administration to a maximal cardiac output or
6 other reliable markers of cardiac function such as stroke volume variation or pulse pressure
7 variation.

Post processing technique

9 For the purpose of this review, a post-processing technique refers to a software package that
10 is used to augment imaging obtained from CT scans, (which are conventionally presented as
11 axial images), to provide additional 2- or 3-dimensional imaging and data relating to an
12 aneurysm's, size, position and anatomy.

Permissive hypotension

14 Permissive hypotension (also known as hypotensive resuscitation and restrictive volume
15 resuscitation) is a method of fluid administration commonly used in people with haemorrhage
16 after trauma. The basic principle of the technique is to maintain haemostasis (the stopping of
17 blood flow) by keeping a person's blood pressure within a lower than normal range. In theory,
18 a lower blood pressure means that blood loss will be slower, and more easily controlled by
19 the pressure of internal self-tamponade and clot formation.

Remote ischemic preconditioning

21 Remote ischemic preconditioning is a procedure that aims to reduce damage (ischaemic
22 injury) that may occur from a restriction in the blood supply to tissues during surgery. The
23 technique aims to trigger the body's natural protective functions. It is sometimes performed
24 before surgery and involves repeated, temporary cessation of blood flow to a limb to create
25 ischemia (lack of oxygen and glucose) in the tissue. In theory, this "conditioning" activates
26 physiological pathways that render the heart muscle resistant to subsequent prolonged
27 periods of ischaemia.

Tranexamic acid

29 Tranexamic acid is an antifibrinolytic agent (medication that promotes blood clotting) that can
30 be used to prevent, stop or reduce unwanted bleeding. It is often used to reduce the need for
31 blood transfusion in adults having surgery, in trauma and in massive obstetric haemorrhage.

32
33