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## Use of rifampicin and graft removal are associated with better outcomes in prosthetic vascular graft infection

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1 2 **Title page**

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**Abstract:**

Objectives: Prosthetic vascular graft infection (PVGI) is a very severe disease. We aimed to determine the factors associated with treatment failure.

Methods: Patients admitted to two University Hospitals with PVGI were included in this retrospective study. PVGI was classified as possible, probable or proven according to an original set of diagnostic criteria. We defined treatment failure if one of the following events occurred within the first year after PVGI diagnosis: death and infection recurrence due to the same or another pathogen.

Results: 112 patients were diagnosed with possible (n=26), probable (n=22) and proven (n=64) PVGI. Bacterial documentation was obtained for 81% of patients. The most frequently identified pathogen was *Staphylococcus aureus* (n=39). Surgery was performed in 96 patients (86%). Antibiotics were administered for more than 6 weeks in 41% of patients. Treatment failure occurred in 30 patients (27.5%). The factors associated with a lower probability of treatment failure were total removal of the infected graft (OR=0.2, 95% CI [0.1-0.6]), rifampicin administration (OR=0.3 [0.1–0.9]) and possible PVGI according to the GRIP criteria (OR=0.3 [0.1–0.9]).

Conclusions: Treatment failure occurred in 27.5% of patients with PVGI. Total removal of the infected graft and rifampicin administration were associated with better outcomes.

66 **Introduction:**

1  
2 67 With a frequency estimated from 1% to 9% [1–4], prosthetic vascular graft infection (PVGI) is  
3  
4 68 a rare complication of vascular surgery associated with severe consequences: the one-year  
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6 69 mortality rate ranges from 19.0% to 34.4% [5–8], and limb amputation can exceed 40% of  
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9 70 patients [9]. Despite this heavy clinical burden, many uncertainties still exist regarding the  
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11 71 optimal management of this infection. PVGI diagnosis is sometimes hard to ascertain, as no  
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13 72 well-defined diagnostic criteria exist. Hence, the conclusions of clinical studies can be biased  
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15 73 if rigorous diagnostic criteria are not applied to include real PVGI patients. In addition, the  
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17 74 available recommendations on PVGI therapy are only based on small case series and expert  
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19 75 opinions [3,10–12]. Medical and surgical treatments should be combined guided by a  
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21 76 multidisciplinary team, but little is known about the specific therapeutic modalities to apply. *In*  
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23 77 *situ* reconstruction with or without graft removal is now thought to be the best surgical option  
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25 78 and is the most frequently performed technique [5,13]. Proposals on the medical treatment of  
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27 79 PVGIs have recently been published, highlighting the need of using molecules active against  
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29 80 bacteria embedded inside the biofilm, but the authors regret the lack of solid evidence  
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31 81 regarding antimicrobial therapy [11].  
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37 82 Thus, our study aimed to determine the occurrence of treatment failure in patients with PVGI  
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39 83 in a large bicentric retrospective study by using a systematic diagnostic method. Secondly,  
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41 84 we searched for factors associated with treatment failure in multivariate analysis.  
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48 **Methods:**

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51 87 **Ethics** The Brest and Rennes ethics committees approved this observational study under  
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53 88 reference numbers 2018CE.21 and 1585, respectively.  
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56 89 **Inclusion** All the patients treated for PVGI in the Brest University Hospital, France, between  
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58 90 January 2011 and June 2016 or in the Rennes University Hospital, France, between January  
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91 2005 and December 2014 were included in this retrospective cohort study. Patients were  
92 identified using the French hospital discharge database. Patients with infection of a biological  
93 graft, a coronary graft or stent, a vascular patch, or a vascular endoprosthesis were excluded.

94 **Definition of PVGI** PVGI was defined according to the *Groupe de Réflexion sur les Infections*  
95 *de Prothèses Vasculaires* (GRIP) criteria [14], displayed in Table 1. Patients were classified  
96 according to the likelihood of PVGI: possible, probable or proven.

97 **Outcome definition** Treatment failure was a composite clinical criterion defined as the  
98 occurrence of one of the following events within the first year after PVGI diagnosis: death due  
99 to PVGI and infection recurrence due to the same or another pathogen during antimicrobial  
100 treatment or after treatment completion. Mortality due to PVGI was assessed by two  
101 independent physicians (MP, SP); in the case of disagreement, the opinion of a third physician  
102 was sought (RLB or MR). Treatment failure was diagnosed according to the GRIP criteria of  
103 PVGI at least 7 days after the initial PVGI diagnosis.

104 **Statistical analysis** Descriptive data were expressed as medians [25<sup>th</sup>–75<sup>th</sup> percentiles] for  
105 continuous variables and as numbers (percentages) for categorical variables. Factors were  
106 tested for association with treatment failure with non-parametric tests. Fisher's exact test was  
107 used for categorical variables, and the Wilcoxon rank sum test was used for continuous  
108 variables. Factors associated with treatment failure in univariate analysis ( $p \leq 0.2$ ) were entered  
109 into a multivariate logistic regression model. Variable selection was performed using backward  
110 and forward selection ( $p \leq 0.05$ ). Adjusted odds ratios were obtained with their 95% confidence  
111 interval [OR (95% CI)]. Analysis was performed using R statistical software, version 3.4.4 [15].

112  
113 **Results:**

114 **Population:**

115 One hundred and twelve patients (81.3% men) were diagnosed with possible, probable and  
116 proven PVGI in 26 (23.2%), 22 (19.6%) and 64 cases (57.1%), respectively. Clinical  
117 characteristics and prognosis of patients according to the likelihood of PVGI are displayed in  
118 the supplementary table. Forty patients (35.7%) were treated at the Brest University Hospital,  
119 and 72 patients (64.3%) in Rennes. The median age was 66 [60-75] years (*Table 2*). The main  
120 cardiovascular risk factors were active smoking (84.3%) and arterial hypertension (60.7%).  
121 The two main comorbidities were coronary artery disease (42.0%) and chronic obstructive  
122 pulmonary disease (28.6%).

123 The site of infection was a peripheral (n=69), an aorto-thoracic (n=15), an aorto-abdominal  
124 (n=24) or an axillo-femoral (n=4) graft. Groin incision was performed at the time of graft  
125 implantation in 92 cases (81.4%). Thirty-one patients (27.7%) needed a second surgery for a  
126 postoperative non-infectious complication.

127 Diagnosis was made after a median time of 51 [16-851] days after graft implantation. At the  
128 time of diagnosis, all patients but three (97.3%) presented with a clinical sign, mainly pain  
129 (65.9%) and fever (62.0%). The C-reactive protein level was >10 mg/L for 92.3% of patients.  
130 Leucocytes were >10 G/L for 67.1% of patients. A CT scan was performed in 58 patients  
131 (51.8%) and contributed to the diagnosis in 89.7% of cases, whereas Doppler was performed  
132 in 15 patients (13.4%) and contributed to diagnosis in 80.0% of cases. Patients with aortic  
133 PVGI presented more frequently with fever than patients with peripheral PVGI (78.6% vs  
134 51.5%,  $p<0.01$ ) and less frequently with local erythema (34.3% vs 65.0%,  $p<0.01$ ).

135 Infections were microbiologically documented in 91 patients (81.3%), including 37 patients with  
136 polymicrobial infection (40.7%). Among patients undergoing surgery with intraoperative  
137 bacterial sampling (n=92), 71 (77.2%) had a positive bacterial culture. Blood culture was  
138 performed in 53 patients (47.3%), and 33 (62.3%) cultures yielded a positive result. One  
139 infection due to *Coxiella burnetii* was documented with positive serology. The most frequent  
140 pathogens are displayed in Table 3 and were gram-positive cocci (62.5%), including

141 *Staphylococcus aureus* (27.3%) and *Enterococcus sp.* (14.6%); gram-negative bacilli (26.4%);  
1 142 and anaerobes (7.7%). The anatomical site of the PVGI did not influence the spectrum of  
2  
3 143 infecting agents and patients with polymicrobial infections did not suffer more frequently from  
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5 144 postoperative wound healing disorders than patients with monomicrobial infections.  
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13 146 **Treatment:**

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16 147 All patients received antimicrobial therapy. Empirical treatment was given to 76 patients  
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18 148 (67.9%), usually a beta-lactam, with an adjunct of an anti-MRSA agent in 46 patients (60.5%).  
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20 149 Twenty-seven patients received antibacterial therapy before intraoperative bacterial sampling  
21  
22 150 for a median duration of 6 [3-14] days. Receiving more than 7 days of antimicrobial treatment  
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24 151 before surgery was associated with negative bacterial culture of intraoperative sampling  
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26 152 (OR=2.44, p=0.02). This effect was not observed for shorter preoperative treatment durations.  
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29 153 The remaining 36 patients were given culture-guided antibiotic therapy directly.  
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32 154 A rifampicin combination was used for definite therapy in 31 patients (27.7%), among whom  
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34 155 21 were infected with *S. aureus*, 7 with coagulase negative staphylococci, 1 with  
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36 156 *Mycobacterium bovis* and 2 with a non-documented infection. The median treatment duration  
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39 157 was 6 [6-9] weeks. Antibiotics were administered for at least 4 weeks in 84 patients (82.6%).  
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41 158 Forty patients (40.8%) received antibiotic therapy for more than 6 weeks, including 8 patients  
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43 159 (7.1%) receiving suppressive lifelong antimicrobial therapy.  
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46 160 Surgical treatment was performed in 96 patients (85.7%). Thirty-eight (33.9%) and ten patients  
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48 161 (8.9%) required a second and a third surgery, respectively. The median time between the  
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50 162 diagnosis of PVGI and the first surgery was 1 [0-6] day. Microbiological optimal surgery (*i.e.*,  
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52 163 total removal of the infected prosthesis) was performed in 48 patients (42.9%). Reconstruction  
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54 164 was needed in 60 patients and was performed with an allograft in 20 cases (20/60, 33.3%), an  
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56 165 autologous vein in 22 cases (22/60, 36.7%) and prosthetic material in the remaining 18  
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58 166 patients. Five patients were treated initially with an endoprosthesis; two of those patients  
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167 required another surgery for total replacement with an allograft. Limb amputation was  
168 performed in 18 cases (16.8%).

169 The factors associated with optimal surgery in univariate analysis were peripheral-arterial  
170 PVGI vs abdomino-thoracic PVGI (47.9% vs 16.7%,  $p=0.02$ ), age (63 vs 66 years old,  $p<0.01$ ),  
171 and year of diagnosis ( $p=0.01$ ). Patients diagnosed with PVGI after 2013 were more likely to  
172 undergo the optimal surgery than patients diagnosed in 2013 or before (56.4% vs 35.6%,  
173  $p=0.04$ ). All-cause mortality did not differ significantly between patients with microbiological  
174 optimal and microbiological non-optimal surgery.

175

176 **Outcome:**

177 All patients but one were followed for more than one year. Three patients (2.7%) and 25  
178 patients (22.3%) died during the first 30 days and the first year after PVGI diagnosis,  
179 respectively. There were no intraoperative deaths.

180 Treatment failure occurred in 30 patients (27.5%) at one year of follow-up. Death due to PVGI  
181 occurred in 12 patients (10.7%), including 3 patients with infection recurrence. Twenty-two  
182 patients (19.6%) presented with infection recurrence that occurred before treatment  
183 completion in 13 cases. For 6 patients (5.4%), infection recurrence was due to another  
184 microorganism and for 15 patients (13.4%) to the same pathogen. The remaining patient  
185 successively presented with these two events. The all-cause mortality rate at one year was  
186 higher in patients with treatment failure (53.3% vs 10.1%,  $p<0.01$ ).

187 According to univariate analysis, the factors significantly associated with a lower risk of  
188 treatment failure were microbiological optimal surgery (Figure), rifampicin administration and  
189 PVGI diagnostic probability as possible vs certain or probable according to the GRIP criteria  
190 (Table 4). No microbiological data were associated with treatment failure.

191 All three factors remained independently associated with a lower risk of treatment failure in the  
192 multivariate analysis: microbiological optimal surgery (OR=0.22 [0.07–0.57],  $p<0.01$ ), possible  
193 PVGI according to the GRIP criteria compared to probable and proven PVGI (OR=0.27 [0.07–  
194 0.85],  $p=0.04$ ), and rifampicin administration (OR=0.30 [0.09–0.87],  $p=0.04$ ). As the diagnosis  
195 of PVGI for the patients classified in the “possible” group could be uncertain, we performed  
196 another multivariate analysis including only the patients with probable or proven PVGI:  
197 microbiological optimal surgery and rifampicin administration remained significantly associated  
198 with a better outcome.

199

## 200 **Discussion:**

201 Important information comes from this large bicentric retrospective study: i) treatment failure  
202 occurred in 27.5% of 112 patients and was associated with a high mortality rate of 53.3% at  
203 one year; ii) use of a rifampicin-combined regimen was associated with a better outcome; and  
204 iii) removal of the entire infected material also.

205 The lack of clear validated diagnostic criteria to define PVGI represents one of the most  
206 problematic issues for improving patient management and literature analysis. In a pioneering  
207 study published in 2005, Fitzgerald *et al* argued for a provisional set of diagnostic criteria, such  
208 as the Duke criteria used for infective endocarditis [12], and an English group of investigators  
209 also recently advocated for this [16]. However, to the best of our knowledge, no study on PVGI  
210 using this kind of diagnostic method has been published so far, and the results of previous  
211 studies can therefore be questioned. We based our work on the diagnostic criteria proposed  
212 by a French multidisciplinary expert group (GRIP) [14] to improve the diagnostic accuracy. We  
213 included all the patients considered to have a PVGI by their treating physicians and then, we  
214 classified all the patients according to the GRIP criteria. PVGI diagnosis likelihood is very high  
215 for patients classified as probable and proven PVGI, but quite low for patients with possible  
216 PVGI. Besides, treatment failure occurred more frequently in patients diagnosed with proven

217 and probable PVGI than in patients with possible PVGI. Our study reflects the real life: due to  
1 218 the severity of the disease, some patients are treated for PVGI even if the diagnosis is not  
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3 219 confirmed. However, our results corroborate the GRIP classification according to diagnostic  
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5 220 probability, and we hope that this systematic method could help physicians to manage this  
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7 221 hard-to-treat infection.  
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11 222 We confirmed that PVGI is a very severe infection, with more than 27% of patients with  
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13 223 treatment failure and an all-cause mortality rate of 22% at one year. Our treatment failure rate  
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15 224 is similar to that of previous reports [5,17,18]. PVGI management relies on a multidisciplinary  
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17 225 approach and requires antibiotic therapy associated with surgical procedures. The best  
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19 226 antimicrobial agents and duration of antibiotic therapy for PVGI remain unknown. Most of our  
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21 227 patients were initially treated with a high dosage of intravenous beta-lactam agents as  
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23 228 recommended [11]. It was impossible to capture the impact of the different initial therapeutic  
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25 229 options; surgical procedures probably had an initial greater impact than antibiotic treatment,  
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27 230 but we found that the use of rifampicin was associated with a better outcome. This has already  
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29 231 been demonstrated for joint-prosthesis infection [19] and for PVGI [5,17]. Rifampicin offers  
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31 232 many advantages in difficult-to-treat infections: high biodisponibility, a large diffusion capacity,  
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33 233 a large spectrum on gram-positive *cocci*, intense bactericidal activity even on intracellular  
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35 234 bacteria [20], and on bacteria with altered metabolic state inside the biofilm [21,22]. In our  
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37 235 work, the rifampicin effect was not differentiated according to the causative pathogen because  
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39 236 of the small sample size. However, rifampicin was essentially used for *S. aureus* PVGI, and  
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41 237 our results add another building block for its importance in material-related *S. aureus*  
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43 238 infections.  
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51 239 One other question regarding the treatment of PVGI refers to the duration of antibiotic therapy.  
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53 240 Available data only come from non-comparative studies whose objectives were not the  
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55 241 evaluation of treatment duration. Most of those publications report 6 or 12 weeks of treatment,  
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57 242 but others report shorter or longer antibiotic therapy. In our study, most patients received  
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59 243 antibiotics for 6 weeks, regardless of whether the surgical treatment was optimal. The survival  
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244 and treatment failure rates were similar to those of other cohorts, and we did not find any  
1 245 impact of treatment duration on treatment failure. Thus, 6-week-long treatment seem to be  
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3 246 long enough for PVGI.  
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6 247 A negative effect of more than 7 days of preoperative antimicrobial therapy was found on the  
7  
8 248 bacterial growth of intraoperative samples. This effect was not observed for shorter treatments  
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10 249 but could be different according to the pathogens and antimicrobial drugs. To minimize the risk  
11  
12 249 but could be different according to the pathogens and antimicrobial drugs. To minimize the risk  
13  
14 250 of perioperative sample culture negativity, preoperative antibiotic therapy should be reserved  
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16 251 for patients with sepsis.  
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19 252 Several techniques have been proposed for the surgical treatment of PVGI. Similar to osteo-  
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21 253 articular infection, total removal of the entire infected graft is encouraged [3,23]. This statement  
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23 254 is supported by little proof [7,24], and some studies have not found this positive impact [5],  
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25 255 sometimes even demonstrating a negative effect [25]. Our study supports the need for this  
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27 256 microbiological optimal surgical treatment in multivariate analysis. However, complete graft  
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29 257 excision is not always possible or can be associated with poor functional results. The choice  
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31 258 of surgical treatment may be guided by the operability of the patient and therefore may be  
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33 259 correlated with the risk of mortality and induced morbidity. In our study, 85.7% of patients  
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35 260 underwent surgery, and 42.9% of patients underwent microbiological optimal surgery with total  
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37 261 removal of the infected vascular prosthesis. Most recent studies reported complete excision of  
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39 262 the infected prosthetic vascular graft in 22.9% to 85.5% of cases [5–7,18]. In our study,  
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41 263 microbiological optimal surgery was more frequently performed in young patients with  
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43 264 peripheral-arterial surgery but did not depend on one specific comorbidity. The surgical rates  
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45 265 increased every year. One explanation for this increasing rate is the recent improvements in  
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47 266 surgical techniques and in anaesthesiology. Performing optimal surgery is now an option in  
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49 267 patients who would have been previously recused. Second, in both participating centres, a  
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51 268 multidisciplinary team that included infectious disease clinicians, surgeons and bacteriologists  
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53 269 was established during the study period.  
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270 There were several limitations in this study. First, this was a retrospective study with all the  
271 associated limitations. However, we used a recognized definition of PVGI using criteria  
272 systematically recorded when taking care of patients with PVGI. Thus, we only included  
273 patients with a high probability of PVGI. In addition, missing data were very rare, and we were  
274 able to collect one-year follow-up data for all the patients except one. Moreover, due to the  
275 scarcity of the disease and the vast heterogeneity of patients, it is very difficult to conduct  
276 prospective multicentre studies in this field. Retrospective cohort studies such as ours are  
277 probably the least incorrect option to improve our knowledge about this very severe disease.  
278 Second, this study included patients with various surgical and medical approaches, but this  
279 reflects the vast heterogeneity of PVGI patient management. We aimed to describe the classic  
280 care of patients with PVGI in real life to draw interesting conclusions in daily practice.

281

## 282 **Conclusion:**

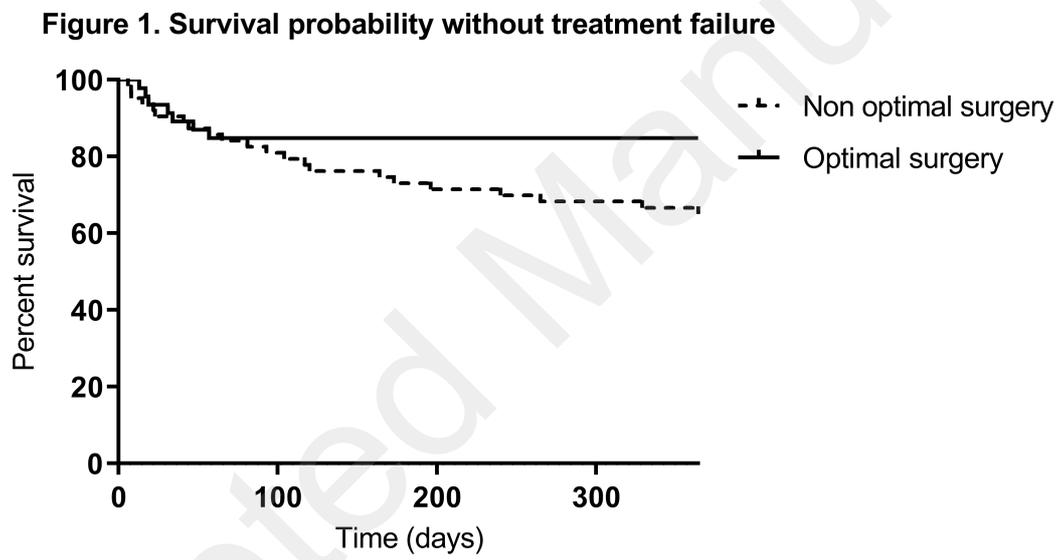
283 In conclusion, PVGI, a biofilm-associated infection, is associated with a high risk of treatment  
284 failure. In this retrospective study, complete excision of the infected graft and rifampicin  
285 administration were associated with favourable outcomes. As complete excision of the graft  
286 constitutes a major surgery, PVGI diagnosis should be based on a recognized definition. Our  
287 study demonstrated the reliability of the GRIP criteria for diagnosis. Prospective studies using  
288 such a definition of PVGI are needed to clarify the best PVGI management choices.

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1 **Tables:**2 **Table 1. *Groupe de Réflexion sur les Infections de Prothèses Vasculaires (GRIP)* diagnostic criteria**

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|   |
|---|
| Proven PVGI:  |
| Two criteria among the following are required: <ul style="list-style-type: none"> <li>• positive smear or culture of intra-operative samples of the vascular prosthesis or periprosthetic tissues</li> <li>• periprosthetic suppuration</li> <li>• presence of collections or periprosthetic air bubbles after eight postoperative weeks</li> <li>• vascular prosthesis exposition through wound or gut</li> </ul>  |
| Probable PVGI:  |
| Two clinical criteria among the following are required: <ul style="list-style-type: none"> <li>• fever, shaking chills, septic shock, or haemorrhagic shock due to aorto-digestive fistula or anastomotic rupture of the bypass</li> <li>• local pain</li> <li>• erythema</li> <li>• local tumefaction</li> <li>• suppurative fistula</li> <li>• abscess or lack of vascular material integration (except PTFE implant)</li> </ul> And a microbiological criterion: <ul style="list-style-type: none"> <li>• one positive blood culture</li> <li>• if commensal flora bacteria are isolated, two positive haemocultures are required</li> </ul> Or a radiological criterion: <ul style="list-style-type: none"> <li>• presence or persistence of collection and/or periprosthetic air bubbles after 8 postoperative weeks</li> <li>• abscess</li> <li>• false aneurysm</li> </ul> |
| Possible PVGI:  |
| One criterion among the following is required <ul style="list-style-type: none"> <li>• a clinical criterion (as listed above)</li> <li>• a biological criterion: C-reactive protein level more than 10 mg/L and/or hyperleukocytosis more than 10 g/L</li> <li>• a radiological criterion (as listed above)</li> </ul>  |

**Table 2. Population characteristics**

| <b>Characteristics</b>                              | <b>Treatment success<br/>(n=82)</b> | <b>Treatment<br/>failure (n=30)</b> | <b>Total (n=112)</b> |
|---|-------------------------------------|-------------------------------------|----------------------|
| Men, <i>n</i> (%)                                   | 68 (82.9)                           | 23 (77.7)                           | 91 (81.3)            |
| Age (years), <i>median</i> [IQ1-IQ2]                | 65 [59-73]                          | 67 [61-78]                          | 66 [60-75]           |
| Diabetes mellitus, <i>n</i> (%)                     | 18 (22.0)                           | 10 (33.3)                           | 28 (25.0)            |
| Chronic obstructive pulmonary disease, <i>n</i> (%) | 23 (28.1)                           | 9 (30.0)                            | 32 (28.6)            |
| Arterial hypertension, <i>n</i> (%)                 | 49 (60.5)                           | 19 (63.3)                           | 68 (60.7)            |
| Coronary artery disease, <i>n</i> (%)               | 33 (40.2)                           | 14 (47.7)                           | 47 (42.0)            |
| Solid cancer, <i>n</i> (%)                          | 20 (24.4)                           | 5 (17.7)                            | 25 (22.3)            |
| Stroke, <i>n</i> (%)                                | 13 (15.9)                           | 2 (6.7)                             | 15 (13.4)            |
| Severe renal insufficiency, <i>n</i> (%)            | 15 (18.3)                           | 7 (24.1)                            | 22 (19.6)            |
| Immunosuppression, <i>n</i> (%)                     | 10 (12.2)                           | 5 (16.7)                            | 15 (13.4)            |
| Active smoking, <i>n</i> (%)                        | 56 (86.2)                           | 19 (79)                             | 75 (84.3)            |
| <b>Presentation at time of diagnosis</b>            |                                     |                                     |                      |
| Fever, <i>n</i> (%)                                 | 50/79 (63.3)                        | 17/29 (58.6)                        | 67/108 (62.1)        |
| Local pain, <i>n</i> (%)                            | 41/60 (68.3)                        | 13/24 (59.1)                        | 54/82 (65.9)         |
| Local erythema, <i>n</i> (%)                        | 37/70 (52.9)                        | 14/25 (56.0)                        | 51/95 (53.7)         |
| Fistula or swelling, <i>n</i> (%)                   | 40/76 (52.6)                        | 17/28 (60.7)                        | 57/104 (54.8)        |
| Scar disunion, <i>n</i> (%)                         | 35/76 (46.1)                        | 9/25 (36.0)                         | 44/101 (43.6)        |
| White blood count > 10 G/L, <i>n</i> (%)            | 47/73 (64.4)                        | 18/24 (75.0)                        | 65/97 (67.0)         |
| C-reactive protein > 10 mg/L, <i>n</i> (%)          | 38/42 (90.5)                        | 15/15 (100)                         | 53/59 (93.0)         |

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**Table 3. Microbiological data**

|  | <b>N (%)</b> |
|--|--------------|
| <b>Bacterial documentation per patient</b>         |              |
| Bacterial documentation                            | 91/112       |
| Polymicrobial PVGI                                 | (81.3)       |
| Positive preoperative samples                      | 37/112       |
| Positive blood samples                             | (33.0) 71/96 |
| <b>Microorganisms isolated (n=144)</b>             | 144 (100)    |
| Aerobic Gram-positive                              | 90 (62.5)    |
| Methicillin-sensitive <i>Staphylococcus aureus</i> | 36 (25.0)    |
| Methicillin-resistant <i>Staphylococcus aureus</i> | 3 (2.1)      |
| Coagulase-negative staphylococci                   | 17 (11.8)    |
| <i>Enterococcus sp.</i>                            | 21 (14.6)    |
| <i>Streptococcus sp.</i>                           | 13 (9.0)     |
| Aerobic Gram-negative bacilli                      | 38 (26.4)    |
| <i>Escherichia coli</i>                            | 12 (8.3)     |
| <i>Pseudomonas aeruginosa</i>                      | 7 (4.9)      |
| Various  | 19 (13.2)    |
| Anaerobes  | 11 (7.7)     |
| <i>Candida sp.</i>                                 | 1 (0.7)      |
| Others   | 4 (2.8)      |

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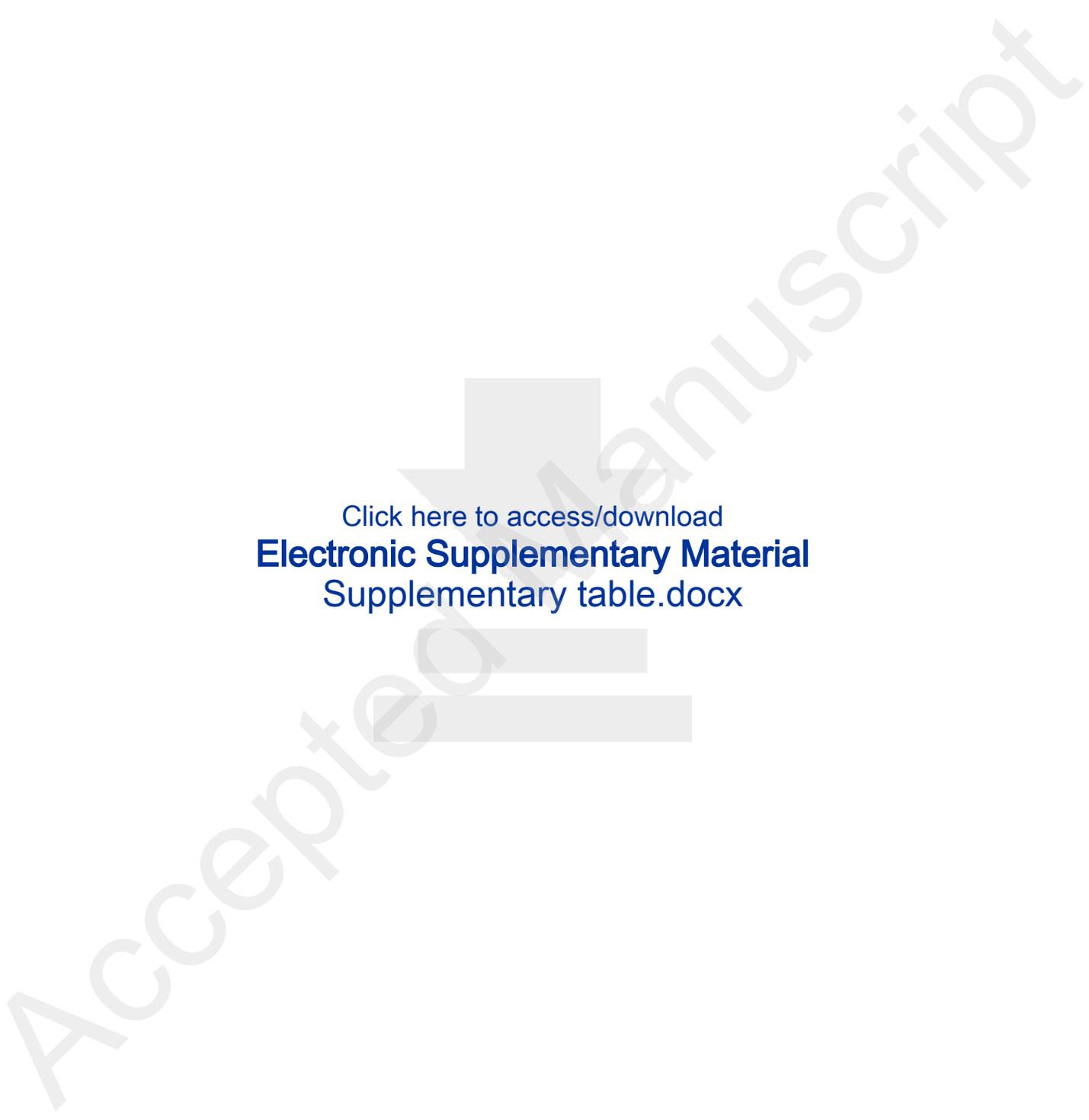
**Table 4. Factors associated with poor outcome in univariate and multivariate analyses**

|  | <b>OR [95% CI]</b> | <b>p-value</b> | <b>OR [95% CI]</b> | <b>p-value</b> |
|--|--------------------|----------------|--------------------|----------------|
| Optimal surgery                        | 0.32               | 0.018          | 0.22 [0.07–0.57]   | p<0.01         |
| Rifampicin administration              | [0.10-0.87] 0.41   | 0.1            | 0.30 [0.09–0.87]   | 0.04           |
| Diagnostic probability (possible PVGI) | [0.11-1.27] 0.40   | 0.13           | 0.27 [0.07–0.85]   | 0.04           |
|  | [0.09-1.36]        |                |                    |                |

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**Supplementary table. Population characteristics according to GRIP definition of PVGI**

| <b>Characteristics</b>                                  | <b>Total (n=112)</b> | <b>Proven or probable PVGI (n=86)</b> | <b>Possible PVGI (n=26)</b> | <b>P-value</b> |
|---|----------------------|---------------------------------------|-----------------------------|----------------|
| Men, <i>n (%)</i>                                       | 91 (81.3)            | 73 (84.9)                             | 18 (69.2)                   | NS             |
| Age (years), <i>median [IQ1-IQ2]</i>                    | 66 [60-75]           | 66 [60-75]                            | 61 [59-73]                  | <0.05          |
| Diabetes mellitus, <i>n (%)</i>                         | 28 (25.0)            | 24 (27.9)                             | 4 (15.4)                    | NS             |
| Chronic obstructive pulmonary disease, <i>n (%)</i>     | 32 (28.6)            | 23 (26.7)                             | 9 (34.6)                    | NS             |
| Arterial hypertension, <i>n (%)</i>                     | 68 (60.7)            | 51 (60.0)                             | 17 (65.4)                   | NS             |
| Coronary artery disease, <i>n (%)</i>                   | 47 (42.0)            | 38 (44.2)                             | 9 (34.6)                    | NS             |
| Solid cancer, <i>n (%)</i>                              | 25 (22.3)            | 19 (22.1)                             | 6 (23.1)                    | NS             |
| Stroke, <i>n (%)</i>                                    | 15 (13.4)            | 14 (16.3)                             | 1 (3.8)                     | NS             |
| Severe renal insufficiency, <i>n (%)</i>                | 22 (19.6)            | 17 (20.0)                             | 5 (19.2)                    | NS             |
| Immunosuppression, <i>n (%)</i>                         | 15 (13.4)            | 12 (14.0)                             | 3 (11.5)                    | NS             |
| Active smoking, <i>n (%)</i>                            | 75 (84.3)            | 59 (83.1)                             | 16 (88.9)                   | NS             |
| <b>Initial surgery</b>                                  |                      |                                       |                             |                |
| Peripheral PVGI, <i>n (%)</i>                           | 69 (61.6)            | 54 (62.8)                             | 15 (57.7)                   | NS             |
| Groin incision  | 92 (81.4)            | 70 (82.6)                             | 21 (80.8)                   | NS             |
| <b>Presentation at time of diagnosis</b>                |                      |                                       |                             |                |
| Fever, <i>n (%)</i>                                     | 67/108 (62.1)        | 54 (65.1)                             | 13 (52.0)                   | NS             |
| Local pain, <i>n (%)</i>                                | 54/82 (65.9)         | 44 (65.7)                             | 10 (66.7)                   | NS             |
| Local erythema, <i>n (%)</i>                            | 51/95 (53.7)         | 40 (54.1)                             | 11 (52.4)                   | NS             |
| Fistula or swelling, <i>n (%)</i>                       | 57/104 (54.8)        | 47 (58.0)                             | 10 (43.5)                   | NS             |
| Scar disunion, <i>n (%)</i>                             | 44/101 (43.6)        | 33 (42.3)                             | 11 (47.8)                   | NS             |
| White blood count > 10 G/L, <i>n (%)</i>                | 65/97 (67.0)         | 51 (68.0)                             | 14 (63.6)                   | NS             |
| C-reactive protein > 10 mg/L, <i>n (%)</i>              | 53/59 (93.0)         | 41 (93.2)                             | 12 (92.3)                   | NS             |
| Microbiological documentation, <i>n (%)</i>             | 91 (81.3)            | 78 (90.7)                             | 13 (50)                     | <0.05          |
| Polymicrobial infection, <i>n (%)</i>                   | 37 (33.0)            | 30 (34.9)                             | 7 (26.9)                    | NS             |
| <b>Treatment and outcome</b>                            |                      |                                       |                             |                |
| Rifampicin-based regimen, <i>n (%)</i>                  | 31 (27.7)            | 25 (29.1)                             | 6 (23.1)                    | NS             |
| Antimicrobial therapy for 6 weeks or more, <i>n (%)</i> | 40 (40.8)            | 32 (41.6)                             | 8 (38.1)                    | NS             |
| Optimal surgery, <i>n (%)</i>                           | 48 (42.9)            | 41 (47.7)                             | 7 (26.9)                    | NS             |
| Death at one year, <i>n (%)</i>                         | 25 (22.3)            | 20 (23.5)                             | 5 (19.2)                    | NS             |
| Treatment failure, <i>n (%)</i>                         | 30 (27.5)            | 26 (31.3)                             | 4 (15.4)                    | NS             |



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