

Ruptured Popliteal Aneurysms: A Case Series and Systematic Review

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Declarations of interest:

None

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Abbreviations:

PAA: Popliteal artery aneurysm, rPAA: Ruptured popliteal artery aneurysm, DVT:” Deep

Venous Thrombosis, VTE: Venous thromboembolism, AAA: Abdominal Aortic Aneurysm,

NNUH: Norfolk and Norwich University Hospital.

25 **Abstract:**

26 **Background:** Ruptured popliteal artery aneurysm (rPAA) is a rare event that represents 2.5% of
27 operated cases of PAA. Many patients present with unilateral leg pain and swelling, therefore
28 often get referred through a variety of pathways, such as DVT clinic.

29 **Objectives:** To evaluate the relationship between the initial diagnosis pathway of rPAA and its
30 influence on outcomes including limb loss and mortality.

31 **Method:** Patients referred to vascular surgery and had a final diagnosis of rPAA between 2007
32 to 2023 were reviewed. Data related to initial diagnosis, time to final diagnosis, limb loss and
33 amputation free survival was recorded. A systematic review was undertaken according to
34 PRISMA guidelines to evaluate reported cases of rPAA.

35 **Results:** Between 2007 and 2022, 40 cases of complicated popliteal artery aneurysms (PAA)
36 requiring intervention were identified in our institute amongst which 6 had rPAA (15%). Initial
37 diagnosis of DVT was suspected in 2 patients with therapeutic anticoagulation commenced prior
38 to vascular evaluation, delaying the diagnosis by up to 6 days. Two patients had early major limb
39 amputations within 90 days of presentation and another 2 had an in-hospital mortality, resulting
40 in a 33.3% amputation free survival. Literature search identified 134 cases of rPAA including
41 case reports and case series. The diagnosis of rPAA was missed in up to 78.89% of the recorded
42 cases and an initial impression of DVT, Baker's cyst rupture, or anticoagulation induced
43 hematoma was made. Mortality was 13.22% within 30 days and almost doubled to 27.68 in 90
44 days. Amputation free survival was 80% and 72% at 30 and 90 days of follow up, respectively.

45 **Conclusion:** Misdiagnosis of rPAA is not uncommon; this will delay diagnosis and proper
46 surgical intervention. Mortality and major amputation are high in this cohort of patients so

47 identification of risk factors and clinical criteria of this cohort can help early diagnosis and
48 proper timely intervention.

49

50 **1. Introduction:**

51 Popliteal artery aneurysm (PAA) is a rare condition in the general population with
52 predominance in men. One study screened hospitalised patients and found the incidence of
53 femoral or popliteal artery aneurysms to be 7.4 per 100,000 men compared to only 1.0 per
54 100,000 women.¹ The prevalence of PAA was found to be less than 1% in more than 1000 men
55 screened in a UK study.²

56 Among asymptomatic patients with PAA, the risk of complications is related to the initial size,
57 mural thrombus load, and the adequacy of the run off vessels. Multiple studies predicted
58 occurrence of symptoms in up to 24% of asymptomatic patients within 2 years and development
59 of complications between 30 to 60% during the patient's lifetime.³⁻⁵ Observational studies have
60 confirmed that aneurysms of larger diameter will enlarge more rapidly and are associated with
61 more complications.⁶ Common symptoms of PAA are related to thrombosis and embolization,
62 with few patients having compression manifestations (DVT and neurological symptoms), and
63 rupture being the least encountered.⁷

64 The incidence of ruptured popliteal artery aneurysm (rPAA) was found to be 2.5% of cases
65 operated for PAA according to a recent Swedish registry [add reference]. The characteristics of
66 PAA that have high risk for rupture are not clear due to rarity of the condition. It is not surprising
67 to find a high prevalence of rupture in larger diameter aneurysms with a mean size of 63mm in
68 the Swedish registry, however, rupture occurred in smaller aneurysms (30mm) and some grew to
69 10cm without rupture. This indicates that other factors can contribute to rupture risk.⁷

70 The main presentation of a rPAA is unilateral leg pain and swelling; these symptoms are non-
71 specific and can have a variety of differential diagnoses. More common clinical entities are
72 likely to be suspected by the physician who will first encounter the patient. Incidental findings of
73 deep venous thrombosis (DVT) was documented in up to 40% of patients with rPAA in a recent
74 systematic review by Akman et al. This is not surprising giving that unilateral leg pain and
75 swelling was the most common presentation (98%).⁸ The aim of this study is to evaluate the risk
76 of misdiagnosis in patients presenting with rPAA and its impact on outcomes including limb loss
77 and mortality.

78

79 **2. Material and Method:**

80 2.1 Protocol: This study was undertaken in 2 parts:

81 2.1.1 Eligibility criteria - case series:

82 A case series was conducted according to PROCESS guidelines⁹. All reported case series with
83 the diagnosis of ruptured popliteal aneurysms were sought. For inclusion, data including
84 symptoms and initial diagnosis were mandatory. Comorbidities, imaging modalities used,
85 intervention details and outcomes were also sought.

86 2.1.2 Eligibility criteria - Systematic review:

87 Systematic review was undertaken in accordance with the Preferred Reporting Items for
88 Systematic Reviews and Meta-Analysis¹⁰. All published case reports with the diagnosis of
89 ruptured popliteal aneurysms were included in the systematic review. Case reports included in
90 prior systematic reviews were retrieved individually. Any case with the diagnosis of popliteal
91 artery aneurysm with no mention of rupture were excluded. English and non-English articles
92 were included. Reports that studied non ruptured popliteal aneurysms or ruptured aneurysms of

93 non-popliteal arteries were excluded. Registries and international studies that lack details on
94 individual cases were excluded.

95 2.2 Information sources:

96 Search was carried out through PubMed/Medline, Ovid, Embase and CINAHL for all reported
97 cases of rPAA using a group of selected terminologies below. We searched the literature from
98 year 1997 to 2023. The last update to our search was conducted on August 2023. The hospital
99 prospectively maintained procedural database was interrogated to identify all cases of popliteal
100 aneurysm between 2007 and 2023. Patients with a final diagnosis of rPAA were included.

101 2.3 Search strategy and study selection:

102 Search terms were selected with the guidance of a librarian including "Popliteal Artery"[Mesh],
103 "Aneurysm, Ruptured"[Mesh], "Embolism and Thrombosis"[Mesh], ruptur*, "Aneurysm".
104 Publications from 1950 to 2023 were included. Eligibility for inclusion was assessed separately
105 by two of the authors (AA, WA) and studies selected according to inclusion criteria, with no
106 discrepancies identified.

107 2.4 Data collection, extraction, and items:

108 All eligible reported articles were retrieved, reviewed, and data extracted individually. Data
109 relating to local hospital patients was also collected. An Excel spreadsheet was created for data
110 collection and included the following variables:

- 111 • Demographics features.
- 112 • Comorbidities, pre-diagnosis anticoagulation state.
- 113 • Presenting symptoms (presence of acute ischemia, DVT, or neurological deficit).
- 114 • Initial assessment site, referrer specialty, duration from presentation to final diagnosis.
- 115 • Imaging modalities, findings, size of PAA.

- Presence of infection or suspicion of mycotic aneurysm.
- Management (surgical, endovascular, or palliative).
- Outcomes.
 - Revascularization patency (30 & 90 days).
 - Major amputation (30 & 90 days).
 - Other complications (30 & 90 days).
 - Survival (30 & 90 days).
- Follow up duration.

2.5 Ethical approval:

In our study, the mentioned cases from our hospital did not reveal any identifiable information, and the systematic review involved literature cases, so ethics approval was not required.

2.6 Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

3. Results:

Examination of our hospital database identified 40 cases of complicated PAA requiring intervention between 2007-2023 amongst which 6 had rPAA. All of them were men aging between 59 to 95 (mean 77.8) with significant medical comorbidities who presented to emergency room with unilateral leg painful swelling. All the patients underwent a confirmatory CT angiogram except one who was taken directly to theatre by orthopaedic team to explore an acute leg hematoma that was found to be a rPAA after which the vascular surgeon was called for

139 assistance. The average size of rPAA was 65 mm. Three patients were on long term therapeutic
140 anticoagulation and 2 started anticoagulation after an initial diagnosis of DVT waiting for a
141 confirmatory duplex ultrasound scan, as per the hospital's VTE protocol. The diagnosis was
142 delayed by 6 days in 1 patient and 2 days in the other. Four patients underwent revascularisation
143 procedures (1 endovascular insertion of covered stent, 2 surgical bypasses, 1 patch repair), the
144 other 2 underwent ligation. The 90-days amputation free survival was 33.33% (2/6; 1
145 endovascular approach and 1 ligation).

146 Literature review identified 66 case reports, 2 case series, and 1 registry. Case reports totalled
147 70 cases, case series totalled 13 cases, and the registry totalled 45 cases. Therefore, 134 cases of
148 rPAA were identified.

149 The mean age of presentation among the 134 cases was 74.95 with the youngest patient being
150 12 years old and the oldest is 96. Most of the patients were men (87.2%) with no side
151 predominance (49.2% on the left side). The most frequent medical comorbidities were
152 hypertension (52%), ischemic heart disease (40%), and chronic kidney disease (39%) Table 1.
153 All patients presented with painful unilateral leg swelling with variable degree of associated
154 symptoms. Acute limb ischemia was present in 19.74% of cases, deep vein thrombosis in 29.1%,
155 and neurological deficits in 14.49% of the cases that mentioned detailed presentation. Among a
156 total of 95 cases, up to 74 patients had an initial diagnosis other than rPAA (Table 2).

157 Given the urgency of the condition and the major consequences on the limb and life, we
158 defined a delayed diagnosis as more than 24 hours from first assessment to vascular
159 referral/intervention. The diagnosis was confirmed within 24 hours in 33 cases (out of 43 cases
160 that reported time to diagnosis) and was delayed more than that in 10 cases ranging from 48
161 hours to 6 days. The source of referral was mentioned in 52 cases (excluding the registry) and

162 was from emergency medicine (55.77%), general practitioners (9.62%), VTE clinic (5.77%), or
163 other specialties including orthopaedics, internal medicine (17.31%). Vascular surgeons were the
164 first to see the patients in 11.54% of the cases.

165 Concomitant AAA was found in 13 out of 43 patients, only 7 underwent a previous repair (5
166 emergency ruptures and 2 electives). The remaining 6 patients were found incidentally on the
167 same admission for rPAA. Four out of the 7 had an intervention within 24 hours, 1 was delayed
168 for a week, and in 2 cases this information was missing. The AAA was over threshold for
169 intervention in 60% (5/8) with an average size of 6.5cm.

170 The mean size for rupture of all rPAA despite the aetiology was found to be 68.3mm among
171 the 134 cases. Interestingly, mycotic aneurysms were found to rupture at a smaller size (mean
172 47.45 +/-15.18) compared to degenerative aneurysms (mean 74.16 +/- 33.89) with a P value
173 0.0131 (Table 3).

174 An intervention was performed in 98.51 % of the cases with revascularization being the most
175 common (83.97% of all interventions). Open bypass is the most frequent approach in the studied
176 cohort reaching up to 74.55% of revascularized cases compared to endovascular stenting
177 (22.73%). Less frequent alternative surgical options included direct repair (1.82 %) and patch
178 anastomosis (0.90%). In the remaining cases who underwent an intervention, surgical ligation or
179 endovascular coiling were performed in presence of adequate collaterals (10.69% and 1.53% of
180 operated cases, respectively), major amputation was done as the initial intervention in 3.79%
181 (Table 4).

182 The 90-day patency of all revascularization procedures in the studied group was 91.30%. A
183 subgroup analysis revealed that among the open revascularization group, 94.4% were patent (34

184 of 36) at 30-days and 90% were patent (27 of 30) at 90-days. In the endovascular group, 89.5%
185 were patent (17 of 19) at 30-days and 94.1% were patent (16 of 18) at 90-days.

186 Major amputations were performed in 4.96% and 12.62% within 30 and 90 days respectively.
187 Mortality was 13.22% within 30 days and almost doubled to 27.68 in 90 days (Table 5).
188 Amputation free survival (AFS) was found to be 80% and 72% in 30 and 90 days of follow up,
189 respectively (fig.1). There was no significant difference in amputation free survival between the
190 delayed and non-delayed groups (7/10 v 14/33, P=0.13).

191 An analysis was done for the complicated presentation including delayed diagnosis/referral
192 (more than 2 weeks) or had unusual symptoms (other than unilateral leg painful swelling). The
193 AFS was 66.7% in this subgroup compared to 76% in patients who presented earlier than 2
194 weeks of symptoms or had typical symptoms of rPAA, despite the initial diagnosis of DVT.
195 However, this difference was found to be statistically insignificant (P 0.44).

196

197 **4. Discussion:**

198 Popliteal artery aneurysms (PAA) represent at least 70% of peripheral aneurysms and appear to
199 occur preferentially in the proximal or midportion of the artery¹¹. Although the major concern in
200 aneurysmal disease is the risk of rupture, in patients with PAA the most common complication is
201 ischemia, and little is known about the few aneurysms that rupture.

202 The clinical presentation of a rPAA relies on the clinical background of the patient, etiology of
203 the aneurysm as well as the extent of the hematoma. The classic presentation is sudden onset
204 pain and swelling behind the knee. Pressure on the adjacent popliteal vein from the haematoma
205 may lead to distal edema or even deep venous thrombosis (DVT) which was confirmed in 29%
206 of the cases that mentioned it.¹² Moreover, 10 out of 40 cases reported the presence of acute

207 neurological deficits on presentation which resulted from nerve compression by the hematoma.

208 Bruising of the surrounding tissues is another manifestation associated with rupture.

209 Embolization and subsequent acute limb ischemia was also found in 17% (12/69).

210 The non-specificity of symptoms makes it likely for non-vascular surgeons to mis-diagnose
211 such an urgent condition. A unilateral leg pain and swelling can be easily diagnosed as DVT and
212 anticoagulant treatment can be commenced which will worsen the situation and cause further
213 delay while waiting for confirmatory scans. Among the reviewed cases, the initial diagnosis was
214 not rPAA in 78% and included DVT (40%), ruptured Baker's cyst, intramuscular hematoma
215 from anticoagulation, hemarthrosis, infected sebaceous cyst, acute limb ischemia and
216 hypovolemic shock. An intraoperative diagnosis was made in one patient who was initially
217 diagnosed as traumatic hematoma with compartment syndrome by the orthopaedic team. Some
218 patients who were confirmed to have ruptured mycotic popliteal aneurysms presented with fever
219 of unknown origin and septic shock.

220 Out of 134 reported cases, only 47 mentioned the specialty of the referrer. From those, only 3
221 cases were first assessed by a vascular surgeon. Delayed diagnosis of rPAA is not infrequent
222 and can be attributed to the rarity of this condition compared to DVT or spontaneous hematoma.
223 Symptoms are not specific and patients are elderly with multiple comorbidities and risk factors
224 for development of DVT. Patients' frailty can make it challenging to obtain a proper history of
225 prior popliteal aneurysms. Clinical vascular examination can also be difficult for the non-
226 specialised, pulses are not easily palpable in the presence of oedema, elderly patients might have
227 asymptomatic peripheral vascular diseases, and a new neurological deficit might be difficult to
228 elicit in diabetic patients with peripheral neuropathy. One of the very specific signs in the studied
229 cases was the presence of subcutaneous ecchymosis that cannot occur with DVT.

230 Another interesting observation in the cohort of patients with rPAA is that up to 36.6% were on
231 anticoagulation at time of diagnosis (15/41). Whether this was related to the initial rupture event,
232 caused delayed thrombosis and so precipitated for rupture or it worsened the symptoms (size of
233 hematoma) is not known.⁷

234 The DVT protocol in our hospital suggests starting anticoagulation treatment for suspected
235 DVT until a confirmatory ultrasound scan is performed at a later date. RPAA can present with
236 associated DVT or can be misdiagnosed as DVT and in both situations patients may be
237 prescribed anticoagulation for up to two weeks prior to establishing a diagnosis of rPAA via an
238 ultrasound scan. In our practice we had 3 patients who presented initially with a DVT and were
239 managed accordingly. Subsequent imaging in the DVT clinic suspected the presence of a
240 hematoma that was confirmed in 24 hours to be a rPAA. Unfortunately, the outcome was poor in
241 those patients. Looking into the whole cohort, there was no significant difference in outcome
242 between delayed and non-delayed cases and that could be due to low numbers (type 1 error).

243 The mean size for rupture was 68.3mm among the 134 cases. It is not surprising to find a high
244 prevalence of rupture in larger diameter aneurysms, however, it is known that even small-
245 diameter PAAs sometimes rupture (30mm) and some grew to 10cm without rupture. Even
246 though the size of an aneurysm is the most important factor predicting rupture risks, many
247 studies and reviews have concluded that other factors can influence the risk of rupture such as
248 wall stress, shape, thrombus load, and metabolic activity.¹³ The presence of infection has been
249 associated with a high risk of rupture AAA.^{14,15} Most of the rPAA that ruptured at size <40mm
250 were mycotic and the ones which continued to grow and ruptured at >80mm were degenerative
251 aneurysms. Majority of mycotic rPAA has ruptured at size <60mm.

252 The difference in rate of amputation and mortality was noticed in our patients who were
253 diagnosed late but that was not replicated in the cohort. Patients who presented with common
254 symptoms and suspected to have DVT or had the diagnosis delayed more than 24 hours did not
255 show difference in outcome compared to the ones who were diagnosed earlier. The difference
256 was seen in the subgroup who were delayed further and had unusual symptoms for at least 2
257 weeks or presented with thigh rather than knee/leg swelling, fever, feeling unwell, acute
258 claudication, neurological deficit with no leg swelling/pain, or collapse. This subset had lower
259 amputation free survival and even though the difference was found statistically non-significant, it
260 still indicates the importance of timely diagnosis and referral specially in unusual symptoms. The
261 worse AFS can also be attributed to the poor clinical condition of the patients.

262 The management of ruptured popliteal aneurysm can be challenging and carries a substantial
263 risk of morbidity and death. Open surgical repair has been the preferred approach. Recent
264 advances in endovascular intervention have continued to push the boundaries of vascular surgery
265 and has been used in emergency cases with ruptured aneurysms and is proving to be an important
266 adjunct to open surgery, particularly in unfit patients, even in the presence of sepsis.¹⁶ On rare
267 occasions where good collateral circulation has developed, the aneurysmal segment can be
268 ligated or embolised.¹⁷

269 We were able to identify High Risk features for rPAA that should raise high index of suspicion if
270 present, those include:

- 271 • Symptoms and signs consistent with DVT
- 272 • Multiple comorbidities
- 273 • Older than 75
- 274 • Prior AAA repair or concomitant AAA

- 275 • Prior PAA repair or concomitant PAA
- 276 • Presence of arterial/neurological symptoms and signs
- 277 • Bruises on examination
- 278 • Young age + Intravenous drug user +/- sepsis
- 279 Recommendations regarding improving diagnostic accuracy of rPAA:
 - 280 • Health care professionals' training in the diagnostic process by educating non-vascular
 - 281 staff (General practitioners and emergency physicians, VTE nurses) about High-risk
 - 282 features:
 - 283 • Lectures, leaflets, posters.
 - 284 • Courses/workshops on how to perform a quick screening popliteal fossa US
 - 285 (popliteal artery enlarged or not).
 - 286 • Early vascular involvement.
 - 287 • Effective teamwork involvement in the diagnostic process among health care
 - 288 professionals & patients:
 - 289 • Diagnostic check list for "leg swelling" cases to be filled looking for high-risk
 - 290 features.
 - 291 • Patient education leaflet for high-risk group (post AAA & post PAA repairs).
 - 292 • Utilize health information technologies in the diagnostic process:
 - 293 • Artificial intelligence (AI)-powered cathbots to ask patients and identify high
 - 294 risk groups, this can help triage patients in emergency settings, prioritize care
 - 295 for GPs, & facilitate early referrals.²⁰
 - 296 • AI probability models to estimate the likelihood of an event using Probability
 - 297 Density Function.²⁰

- Conduct researches on the diagnostic processes and errors

The limitations of this study should be acknowledged. Firstly, cases were retrospectively enrolled, which is not free from a recall bias. However, we adjusted the variance to avoid any confounding effects. Secondly, not all cases were reported so there was reporting bias. Thirdly, there was only one large case series included in the study which could limit the generalisability. Finally, not all information were available for all outcomes, which increased the risk of selection bias.

5. Conclusion:

Ruptured PAA is an uncommon condition that should be suspected in individuals who present with symptoms of DVT specially if the patient is an elderly (>70) male with multiple comorbidities. Special attention should be made if bruises are seen on examination or if the patient is already on therapeutic anticoagulation. The rate of major amputation and mortality is high in this group (despite the initial diagnosis of DVT) and early diagnosis and referral depends on high index of suspicion.

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