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1 **Characteristics and Risk Factors for Poor Outcome in Patients with** 2 **Systemic Vasculitis Involving the Gastrointestinal Tract.**

3

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53

54 **Abbreviations:** GI: gastrointestinal; ICU: intensive care unit; FFS: Five Factors Score; PAN:
55 polyarteritis nodosa; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis ;
56 EGPA: eosinophilic granulomatosis with polyangiitis; GCA: giant-cell arteritis; IgAV: IgA
57 vasculitis; CryoVas: cryoglobulinemia vasculitis; CT: computed tomography; SAPS:
58 simplified acute-physiology score; CRP: C-reactive protein; AAV: ANCA-associated
59 vasculitides; LDH: lactate dehydrogenase.

60 **Authorship Statement**

61 • Dr Gendreau, and Pr Terrier: Conceptualization; Data curation; Formal analysis;
62 Investigation; Writing - original draft; Writing - review & editing.

63 • Dr Gendreau, Pr Terrier, Dr Porcher : Methodology; Analysis and interpretation of data

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68 Guillevin: Design of the study; Data curation; Writing - review & editing.

69 All authors approved the final version of the article, including the authorship list.

70

71

72 **Abstract**

73 **Background:** Gastrointestinal (GI) involvement was described to be a poor prognostic factor
74 in systemic necrotizing vasculitis. Its prognostic significance may vary according to clinical
75 presentation and vasculitis subtype.

76 **Aims:** This study investigated risk-factors associated to poor outcome in GI-involvement of
77 vasculitis.

78 **Methods:** Patients with systemic vasculitis as defined by the 2012 Chapel Hill Consensus
79 Conference and presenting with GI involvement were retrospectively included. Baseline
80 characteristics, treatments and outcome were recorded. Primary endpoint was a composite of
81 admission to intensive care unit (ICU), emergency surgical procedure, or death.

82 **Results:** Two hundred and thirteen patients were included. Vasculitis were distributed as
83 follows: 41% IgA vasculitis, 27% ANCA-associated vasculitis, 17% polyarteritis nodosa
84 (PAN), and 15% other vasculitis. Eighty-three (39%) patients fulfilled the composite primary
85 endpoint within 6 months. Predictive factors associated with the primary endpoint included
86 PAN subtype (OR 3.08, 95% CI 1.29-7.34), performance status (OR 1.40, 1.05-1.87), use of
87 morphine (OR 2.51, 0.87-7.24), abdominal guarding (OR 3.08, 1.01-9.37), ileus (OR 2.29,
88 0.98-5.32), melena (OR 2.74, 1.17-6.42), increased leukocytes (per G/L, OR 1.05, 1.00-1.10),
89 low hemoglobin (per g/dL, OR 0.80, 0.71-0.91) and increased CRP (log mg/L, OR 1.21, 0.94-
90 1.56). A risk prediction model for the achievement of primary endpoint had a very good
91 performance [C-statistics 0.853 (0.810 to 0.895)], and for overall survival as well.

92 **Conclusions:** Vasculitis presenting with GI involvement have a poor outcome in more than
93 one third of cases. An easy-to-use risk prediction model had a very good performance to
94 predict the admission to ICU, emergency surgical procedure, or death.

95

96 **Keywords:** Risk Factors; Systemic Vasculitis; Gastrointestinal Tract; intestinal ischemia;

97 **1. Introduction**

98 Systemic vasculitis are inflammatory diseases of the blood vessel wall, defined in the
99 2012 revised Chapel Hill Consensus Conference according to the size and the type of
100 involved vessels[1]. Gastrointestinal (GI) involvement may occur with a frequency ranging
101 from 10 to 50% according to the type of vasculitis. While its presentation is often nonspecific,
102 GI involvement represents a severe and life-threatening condition, which requires an early and
103 immediate management to decrease morbidity and mortality [2]. Severe GI involvement is
104 identified as a poor prognostic factor in the Five Factors Score (FFS)[3].

105 A previous study from our group described in 2005 the GI involvement in necrotizing
106 systemic vasculitides[4]. Amongst 62 patients, factors associated with death were peritonitis
107 (hazard ratio [HR] = 4.3, $p < 0.01$), bowel perforation (HR = 5.7, $p < 0.01$), intestinal
108 occlusion (HR = 5.5, $p < 0.01$), and intestinal ischemia (HR = 4.1, $p < 0.01$). However, this
109 study did not include other vasculitis subtype, and the admission to intensive care unit (ICU)
110 or surgery were not analyzed whereas they represent more frequent outcomes.

111 Since GI involvement remains a life-threatening condition despite the significant
112 improvement of vasculitis management, we investigated GI involvement in the current era to
113 identify prognostic factors for the admission to the ICU, surgery or death, and develop a risk
114 prediction model to assist the therapeutic decision.

115

116 **2. Material and methods**

117 **2.1 Inclusion criteria**

118 We retrospectively included patients with systemic vasculitides diagnosed between January
119 2006 and May 2019 according to the 2012 Chapel Hill Consensus Conference [1], and
120 presenting with GI involvement. Systemic vasculitides included including polyarteritis nodosa
121 (PAN), microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA),

122 eosinophilic granulomatosis with polyangiitis (EGPA), giant-cell arteritis (GCA), Takayasu
123 disease, Behçet disease, IgA vasculitis (IgAV), cryoglobulinemia vasculitis (CryoVas) and
124 hypocomplementemic urticarial vasculitis.

125 Cases fulfilling inclusion criteria were selected from the French Vasculitis Study Group
126 (FVSG) database in one hand,, and also by contacting all vasculitis practitioners registered
127 within the FVSG network for additional cases in the other hand [12].Patients were from
128 centers in France and Belgium, including internal medicine, intensive care unit, nephrology,
129 rheumatology and dermatology departments. GI involvement was defined as follows: GI
130 symptom associated with radiologic or endoscopic findings[5–7] consistent with intra-
131 abdominal vasculitis, or GI manifestations[8–11] present at vasculitis' diagnosis or relapse
132 and responding to specific immunomodulatory agents. GI involvement could occur at
133 vasculitis onset or during a relapse. Patients were excluded if GI involvement could not be
134 explained by vasculitis itself.

135 This study was conducted in compliance with the Good Clinical Practice protocol and the
136 Declaration of Helsinki principles and was approved by the local ethics committee
137 Institutional Review Board from Cochin Hospital, Paris (CLEP Decision N°: AAA-2020-
138 08036).

139 **2.2 Data collection**

140 Each physician fulfilled a standardized case report form for submission of cases.
141 Medical files were reviewed for gender, age, past medical history (cirrhosis, embolic or pro-
142 thrombotic diseases, cancer, previous history of gastric ulcer, or anticoagulation or antiplatelet
143 therapy), vasculitis presentation at diagnosis and during relapse (weight, size, fever, asthenia,
144 arthralgia, weight loss >10%, cutaneous, ear, nose and throat, ocular, pulmonary, renal,
145 neurological and cardiac manifestations). Gastrointestinal symptoms included abdominal pain,
146 abdominal guarding, nausea or vomiting, diarrhea, ileus, hematemesis, melena or rectal
147 bleeding. GI manifestations were assessed on clinical examination at admission and during

148 hospital stay. GI involvement was defined on computed tomography (CT) scan or any other
149 imaging performed, or endoscopic evaluation. Inflammation of the bowel wall was defined by
150 colitis, gastritis, or any GI parietal abnormalities described as such on either imaging or
151 endoscopic procedure. Inflammation of digestive arteries were assessed on CT scan or
152 angiography. Two prognostic scores were collected from medical files, *i.e.* performance status
153 [13] at admission and simplified acute-physiology score (SAPS) [14] assessed during the first
154 24 hours of hospital admission.

155 Biological data included C-reactive protein (CRP), serum levels of IgA for IgAV, and ANCA
156 serotype for ANCA-associated vasculitides (AAV). Standard biology was also recorded on
157 admission (leukocytes, neutrophils, lymphocytes, hemoglobin level, fibrinogen, lactate
158 dehydrogenase (LDH) and albumin levels, liver function tests). Radiological and endoscopic
159 features were recorded according to previous studies[5–7], and GI biopsies were provided
160 when performed.

161 Treatment of vasculitis included glucocorticoids, immunosuppressive and/or
162 immunomodulatory drugs[15], and symptomatic treatments. Interventional endoscopy or
163 radiology, surgery, antibiotic therapy, transfusion therapy, and antiplatelet or anticoagulation
164 therapy were recorded. Each case report form was reviewed by SG and BT. The data
165 underlying this article cannot be shared publicly, for the privacy of individuals that
166 participated in the study. The data will be shared on reasonable request to the corresponding
167 author.

168 **2.3 Outcome**

169 The primary endpoint was a composite of admission to ICU, emergency surgical
170 procedure, or death within 6 months from hospital admission. Secondary endpoints were the
171 description of the spectrum of systemic vasculitis and their presentation, the characteristics
172 associated with GI involvement, and the overall prognosis of GI involvement. Refractory
173 vasculitis was defined by a disease uncontrolled by standard treatment[16].

174 **2.4 Statistics**

175 Data are reported as numbers and percentages for categorical data and mean and standard
176 deviation (SD) or median and interquartile range (IQR) for quantitative data, except otherwise
177 stated. Extensive informations on statistical analysis are indicated in the **Supplementary**
178 **material**. Missing baseline data were handled through multiple imputations. We used logistic
179 regression, and three strategies were adopted for model development with the imputed data.
180 Model performance was evaluated both by the concordance (c) statistic, as a measure of
181 discrimination, and the calibration curve. The c statistic quantifies how well the model
182 discriminates between patients dying and those surviving, and can be viewed as the extension
183 of the area under the receiver operating characteristics (ROC) curve for survival data[17]. It
184 varies between 0.5 and 1.0, where 1.0 indicates perfect discrimination. The calibration curve
185 contrasts observed versus predicted probabilities of event to evaluate the accuracy of model
186 predictions. The slope of the calibration curve is a measure of optimism of model predictions.
187 A receiver-operating characteristics (ROC) curve was also used to illustrate the ability of the
188 model to discriminate between patients with and without occurrence of the outcome. Last,
189 decision curve analysis (DCA) was used to assess the incremental value of the risk prediction
190 model for medical decision making. Since prognostic models derived from multivariable
191 regression with variable selection are prone to overestimate regression coefficients, internal
192 validation of our model was carried out using bootstrap. The final model was presented with
193 odds ratios obtained after shrinkage and their 95% confidence intervals (95% CI), and a
194 nomogram to allow an easier calculation of the prediction score. All tests were two-sided.
195 Analyses were performed using the R statistical software version 3.6.1[18].

196

197

198 **3. Results**

199 **3.1 Patients' characteristics**

200 A total of 213 patients (66% male, median age 50 years) were included from 31
201 centers. Baseline characteristics are presented in **Tables 1 and 2**. Eighty-seven (40.8%)
202 patients had IgAV, 36 had PAN (16.9%) and 58 patients presented AAV (27.2%). Other
203 vasculitis included GCA CryoVas, Takayasu arteritis, Kawasaki disease, Behçet disease, or
204 unclassified vasculitis.

205

206 **Table 1. Characteristics of patients and vasculitis manifestations on hospital admission**
 207 **in the 213 patients.**

Characteristics	Overall population (n=213)
Age (year) – median (range)	51 (14 to 94)
Female gender, No. (%)	72 (33.8)
Type of vasculitis, No. (%)	
IgA vasculitis	87 (40.8)
PAN	36 (16.9)
GPA	30 (14.1)
EGPA	15 (7.0)
Microscopic polyangiitis	13 (6.1)
Cryoglobulinemia	10 (4.7)
Others	22 (10.3)
GI involvement at diagnosis, No. (%)	164 (77.0)
BMI, median [IQR], kg/m²	23.2 (20.2 to 27.5) (n=190)
Constitutional symptoms, No. (%)	
Asthenia	134 (62.9)
Arthralgia	82 (38.5)
Weight loss	65 (30.5)
Fever	46 (21.6)
Myalgia	27 (12.7)
Arthritis	26 (12.2)
Other organ involvement, No. (%)	
Skin involvement	125 (58.7)
Renal involvement	97 (45.5)
Head and neck	42 (19.7)
Pulmonary involvement	39 (18.3)
Peripheral neurological	39 (18.3)
Central neurological	18 (8.5)
Heart involvement	16 (7.5)
Eye involvement	12 (5.6)

208 Data are presented as median (interquartile range, 25th-75th percentiles) or number

209 (percentage); EGPA: Eosinophilic granulomatosis with polyangiitis; GPA: Granulomatosis

210 with polyangiitis; PAN: Polyarteritis nodosa; GI: gastro-intestinal.

211

212 **Table 2. Characteristics of GI manifestations on hospital admission in the 213 patients.**

Characteristics	Overall population	N
Previous GI symptoms, No. (%)	83 (39.0)	213
Parameters on admission, median [IQR]		190
Systolic blood pressure (mmHg)	129 (115 to 144)	
Diastolic blood pressure (mmHg)	75 (65 to 84)	
Peripheral oxygen saturation (%)	98 (97 to 100)	
Body temperature (°C)	37.0 (36.7 to 37.2)	
Heart rate (bpm)	86 (75 to 101)	
Performance status, No. (%)		204
PS 0	33 (16.2)	
PS 1-2	123 (60.3)	
PS 3-4	48 (23.5)	
GI manifestations, No. (%)		213
Abdominal pain	189 (88.7)	
Diarrhea	62 (29.1)	
Rectal bleeding	53 (24.9)	
Nausea/vomiting	52 (24.4)	
Melena	32 (15.0)	
Ileus	28 (13.1)	
Guarding or peritonism	26 (12.2)	
Hematemesis	11 (5.2)	
SAPS-II score, median [IQR]	18 (13 to 24)	194
Biological data, median [IQR]		
White blood cell count (G/L)	12.0 (8.7 to 16.5)	183
Neutrophil count(G/L)	8.5 (5.9 to 12.1)	142
Lymphocyte count (G/L)	1.5 (1.0 to 2.2)	124
Hemoglobin (g/dL)	11.6 (9.4 to 13.8)	186
Creatinine, µmol/L	79.0 (62.0 to 119.5)	174
C-reactive protein (mg/L)	59.1 (18.6 to 115.0)	183
Fibrinogen (g/L)	4.8 (4.0 to 6.0)	97
Lactate dehydrogenase (UI/L)	256.0 (179.2 to 409.8)	96
Albumin (g/L)	30.5 (23.9 to 38.0)	114
HCO ₃ ⁻ (mmol/L)	24.8 (22.0 to 26.4)	132
GI involvement, No. (%)		213
Inflammation of the bowel wall	144 (71.6)	
Peritonitis	21 (10.4)	
Bowel wall hematoma	12 (6.0)	
Splenic or hepatic infarction	10 (4.9)	
Cholecystitis	6 (3.0)	
Pancreatitis	5 (2.5)	
Invagination	2 (1.0)	
Appendicitis	1 (0.5)	

213 Data are presented as median [25th-75th percentiles] or number (percentage); SAPS-II:

214 Simplified Acute Physiology Score. N: number of observations available.

215

216 **3.2 Clinical manifestations**

217 On hospital admission, 65/213 (30.5%) had weight loss >10% and 46/213 (21.6%)
218 presented with fever. Clinical and biological presentation are summarized in **Table 1**. Main
219 organ involvement included cutaneous (58.7%), renal (45.5%), neurological (26.8%),
220 pulmonary (18.3%) and heart involvement (7.5%). GI manifestations and diagnoses are
221 reported in **Table 2**. Briefly, GI manifestations occurred at vasculitis diagnosis in 164/213
222 (77%) patients, and 83/213 (39%) experienced previous transient GI manifestations before
223 diagnosis. Clinical presentation included abdominal pain in 88.7%, requiring morphine in
224 10.3%, GI bleeding in 34.7% with hematemesis (11/213, 5.2%), melena (32/213, 15%) and/or
225 rectal bleeding (53/213, 24.9%), diarrhea in 29.1%, nausea or vomiting in 24.4%, ileus in
226 13.1%, abdominal guarding in 9.4% or peritonism in 2.8%. Amongst patients with GI
227 bleedings, median hemoglobin was 10.9 g/dL [IQR 8.5-13.0], and 32.9% (24/73) received red
228 blood cell transfusion.

229 Endoscopic procedures were performed in 112 (53.3%) patients, showing evidence of
230 mucosal alterations in 81 (72.3%). Other investigations included CT scan in 81%,
231 ultrasonography in 11.4%, angiography in 5.7%, and 76 (35.7%) patients had either
232 endoscopic or surgical biopsy.

233 Overall, final diagnoses for GI involvement are summarized in **Table 2**, and included
234 inflammation of the bowel wall in 71.6%, intestinal ischemia in 16.5% (ischemic colitis in 9%
235 and ischemic small bowel disease in 7.5%), peritonitis in 10.4%, bowel perforation in 10.9%
236 (involving the small intestine in 8%, large bowel in 3% and the stomach in 2%). Abnormal
237 digestive arteries were noted in 40 (20%) patients.

238

239 **3.3 Treatments and outcomes**

240 Among the 213 patients, 192 (91%) received glucocorticoids (including pulses of
241 methylprednisolone in 52.9%), with an initial median dose of 1.0 mg/kg/day (IQR 0.9-1.0),

242 and 140 (66.4%) immunosuppressive or immunomodulatory drugs (cyclophosphamide in
 243 45.2%, rituximab in 16.2%, therapeutic plasma exchange in 13.8%) (**Table 3**).

244 The primary endpoint, *i.e.* admission to ICU, surgery and/or death within 6 months, was
 245 achieved in 83 (39%) patients (**Table 3**), including ICU admission in 31.9%, surgery in
 246 19.7%, and death in 8.5%. Among the patients admitted to the ICU, 40.3% underwent
 247 mechanical ventilation (intubation for surgical purposes were not considered), 33.8% had
 248 shock requiring amines, 26.5% had renal replacement therapy and 1.5% required extra-
 249 corporeal membrane oxygenation. Other interventions included interventional endoscopy
 250 (4.7%) and radiology (3.3%). Finally, 18.6% patients received transfusion.

251

252 **Table 3. Treatment, outcome and follow-up of GI manifestations of vasculitis in the 213**
 253 **patients.**

Characteristics	Overall population	N
Composite outcome achieved, No. (%)	83 (39.0)	213
ICU admission	68 (31.9)	
Surgery	42 (19.7)	
Death	18 (8.5)	
Treatments and supportive care, No. (%)		
Initiation of immunosuppressive therapy	201 (95.3)	211
Glucocorticoids	192 (91)	
Pulses of methylprednisolone	111 (57.8)	
Cyclophosphamide	95 (45.2)	
Rituximab	34 (16.2)	
Therapeutic plasma exchange	29 (13.8)	
Interventional endoscopy	10 (4.7)	212
Interventional radiology	7 (3.3)	212
Red blood cell transfusion	39 (18.6)	210
Status at 6-month follow-up, No. (%)		
Refractory disease	17 (10.1)	169
Persistent GI symptoms	26 (15.4)	169
Stomia during episode	24 (11.4)	213
Definitive stomia	5 (22.7)	
Vasculitis relapse	40 (23.4)	170
GI relapse	17 (10.0)	170

254 Data are presented as median [25th-75th percentiles] or number (percentage); ICU: intensive-
 255 care unit; GI: gastro-intestinal. N: number of observations available.

256

257 **3.4 Risk factors for poor outcome**

258 In univariate analysis, the following factors were associated with the achievement of
259 the primary endpoint: diagnosis of PAN, age, fever, neurological or cardiac manifestations,
260 requirement for morphine, abdominal guarding, ileus, melena, peritonitis, low oxygen
261 saturation, high CRP, increased leukocytes, low hemoglobin level, and a high SAPSII score.

262 We next aimed to define a risk prediction model. The final model retained the type of
263 vasculitis, performance status, use of morphine, abdominal guarding, ileus, melena, white
264 blood cell count, hemoglobin and CRP (**Table 4**). A nomogram described the scoring system
265 based on these characteristics was set up, with each item being associated to points according
266 to its value (**Figure 1**). The sum of point was associated with the predicted probability of
267 admission to the ICU, surgery or death during the first 6 months (see **Supplementary Figure**
268 **1**). C statistics for this model was 0.853 (0.810 to 0.895) (see **Supplementary Figure 2 and**
269 **3**). The net benefice of intervention according to the scoring system was strongly in favor of
270 using the risk-prediction model over a treat-none strategy (see **Supplementary Figure 4**).

271 During follow-up (median 24 months, IQR [10-59]), 25 (11.7%) patients died. Overall
272 survival was associated with the prediction score, with a C statistic of 0.735 (95% CI: 0.648 to
273 0.822). Overall survival was markedly different between the three tertiles of predicted
274 probabilities (**Figure 2**). Finally, 26/168 (15.4%) patients had persistent abdominal symptoms
275 after treatment, mainly abdominal pain in 57.7% and diarrhea in 34.6%. Vasculitis flares at 6-
276 months occurred in 23.4% during follow-up, including GI flares in 10.0% (**Table 3**).

277

278 **Table 4. Associations between baseline factors and primary outcome (ICU admission,**
 279 **surgery for worsening or death within 6 months).**

Variable	Full multivariable model		Final model	
	OR (95% CI)	P	OR (95% CI)	P
PAN	3.82 (0.99 to 14.8)	0.05	3.08 (1.29 to 7.34)	0.01
Non-IgA, non-PAN vasculitis	3.23 (1.07 to 9.69)	0.04	2.14 (1.05 to 4.36)	0.04
Female	0.88 (0.37 to 2.12)	0.8	-	-
Age (per year)	1.00 (0.98 to 1.03)	0.7	-	-
Fever	1.02 (0.40 to 2.64)	0.97	-	-
Weight loss	0.84 (0.35 to 2.06)	0.7	-	-
Performance status (per score point)	1.60 (1.05 to 2.45)	0.03	1.40 (1.05 to 1.87)	0.02
Use of morphine	3.36 (0.78 to 14.5)	0.1	2.51 (0.87 to 7.24)	0.09
Guarding	5.07 (1.03 to 24.9)	0.05	3.08 (1.01 to 9.37)	0.05
Ileus	3.15 (0.93 to 10.7)	0.07	2.29 (0.98 to 5.32)	0.05
Melena	4.61 (1.33 to 16.0)	0.02	2.74 (1.17 to 6.42)	0.02
White blood cell count (per G/L)	1.08 (1.00 to 1.16)	0.06	1.05 (1.00 to 1.10)	0.07
Hemoglobin (per g/dL)	0.74 (0.62 to 0.88)	<0.001	0.80 (0.71 to 0.91)	<0.001
C-reactive protein (mg/dL, as log)	1.07 (0.97 to 1.18)	0.2	1.21 (0.94 to 1.56)	0.1
Inflammation of the bowel wall	1.17 (0.51 to 2.70)	0.7	-	-
Inflammation of digestive arteries	1.95 (0.73 to 5.21)	0.2	-	-

280 Odds ratios are pooled over the 30 imputed datasets. Odds ratios for the final model are

281 shrunk by the calibration slope (0.73). PAN: Polyarteritis nodosa.

282

283 **Figure 1: Nomogram to predict the risk for ICU admission, surgery for worsening or**
284 **death within 6 months.**

285 The nomogram conveys the result of the risk prediction model by allowing the calculation of
286 the estimated probability of death according to patient characteristics. For each characteristic
287 on the figure, locate the value of the axis and draw a straight line up to the point's axis on the
288 top of the figure, to determine how many points the patient should receive. Sum the points
289 received for all characteristics, and locate this number of the total point's axis. Draw a straight
290 line down from the total points to the predicted probability axis.

291

292

293 **Figure 2. Overall survival according to the risk prediction model.**

294 The risk prediction model is divided into three approximately evenly sized groups. The x-axis
295 corresponds to time, in months.

296

297

299 **4. Discussion**

300 In this study, 83/213 (39%) patients with systemic vasculitis involving the GI tract
301 had a poor outcome, defined as the admission to the ICU, surgery and/or death. We therefore
302 analyzed risk factors for poor outcome and identified a prognostic role of the type of
303 vasculitis, baseline performance status, abdominal pain requiring morphine, abdominal
304 guarding, ileus, melena, leukocyte count, hemoglobin and CRP levels. These features enabled
305 the development of a scoring system that accurately quantify the predicted risk for a poor
306 outcome.

307 Although the 5-year survival rate in systemic necrotizing vasculitides significantly
308 increased between 1990 and the last decade[2], GI complications remain the third cause of
309 vasculitis-related death, after multi-organ failure and pulmonary complication[3]. However,
310 the definition of severe GI involvement remains unclear and GI manifestations and its severity
311 may differ between vasculitis subtypes, variable that was not included in previous prognostic
312 studies. In our study, the primary endpoint was achieved in 18/87 patients (21%) in IgAV,
313 28/57 patients (48%) in AAV and 24/36 patients (67%) in PAN. These results are in
314 accordance with previous data in IgAV[19], where GI involvement was noted in 48%, but
315 severe manifestations requiring transfusion, surgery or leading to death were noted in only
316 11%. In contrast, in PAN, AAV and rheumatoid arthritis-associated vasculitis[4], death was
317 more frequently reported, occurring in 26% of patients with GI manifestations, with
318 peritonitis, bowel perforation, intestinal occlusion and intestinal ischemia being significantly
319 associated with this outcome[4]. The clinical factors that we evidenced in our study (*i.e.*
320 abdominal pain requiring morphine, abdominal guarding, ileus, melena) are strongly
321 suggestive of these severe complications, and are more easily applicable in daily practice.
322 Also, prognostic factor as performance status, associated with our primary endpoint, is an
323 easy and reliable tool to identify patients' fragility. Of note, age >65 years was not

324 significantly associated with the primary endpoint in our study. We could assume that the
325 wild range of age in our study population and the adjustment with vasculitis subtype and GI
326 manifestations could be an explanation.

327 We aimed to develop a scoring system to estimate the risk of poor outcome in patients
328 with GI involvement. Main objectives were to better identify patients at high-risk of clinical
329 deterioration, and eventually to improve patient management by considering aggressive
330 therapeutic strategies in the most severe patients, since infections were shown to account for
331 30% of deaths in the ICU[20]. Initiating aggressive treatments could be difficult in patients at
332 risk of clinical deterioration, but delayed initiation of cyclophosphamide was associated with
333 an increased risk of death in this severe population[20]. Overall, we think that clinical and
334 biological items from our risk prediction model accurately and early identify patients prone to
335 clinical deterioration, and thus who should benefit from early assessment by the intensivists
336 and preemptive admission to the ICU. The score we developed is easy to calculate within the
337 first 24 hours of admission to orientate high-risk patients, and it could also alleviate the use of
338 aggressive treatments in patients at lower risk, such as non-severe IgAV patients in which the
339 use of immunosuppressive agents for GI involvement is not clearly established.

340 Our study has some limitations. The retrospective design over a long time period
341 could be associated with a lack of homogeneity into supportive care and treatments used.
342 However, glucocorticoids, cyclophosphamide and rituximab were the most frequently used
343 treatments, which still represent the standard of care for such patients[19,21]. Also, because of
344 the retrospective design, although large and multicentric, our findings and especially our score
345 should be validated prospectively and on a different cohort of patients. Vasculitis were mainly
346 represented by IgAV, AAV and PAN, and other vasculitis were lacking (large vessels
347 vasculitis, cryoglobulinemia vasculitis, Behçet disease), explaining why our data should be
348 interpreted cautiously in these vasculitis types. Of the 213 participants of the study, definitive
349 information was missing for 3 who were discharged alive from hospital, and lost to follow-up
350 at one month (n=2) or three months (n=1): we considered those 3 patients did not experience

351 the outcome at 6 months, as it would be most unlikely that those patients would have
352 experienced for the outcome without the team caring for their vasculitis being notified.
353 Finally, since this retrospective study was based on reported cases, we cannot exclude an
354 overestimation of severe cases and poor outcomes in the different vasculitis subtypes, due to
355 memory biases.

356

357 **5. Conclusions**

358 In conclusion, systemic vasculitis involving the GI tract still have a poor outcome in
359 more than one third of cases, mainly in case of PAN. Routinely evaluated clinical and
360 biological parameters on admission are associated with a poor outcome and can be included in
361 a score that accurately predict the risk for admission to the ICU, surgery and/or death. These
362 risk factors assessed during the first hours could help the physicians to manage vasculitis
363 patients with GI involvement and should be validated in a prospective study.

364

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370

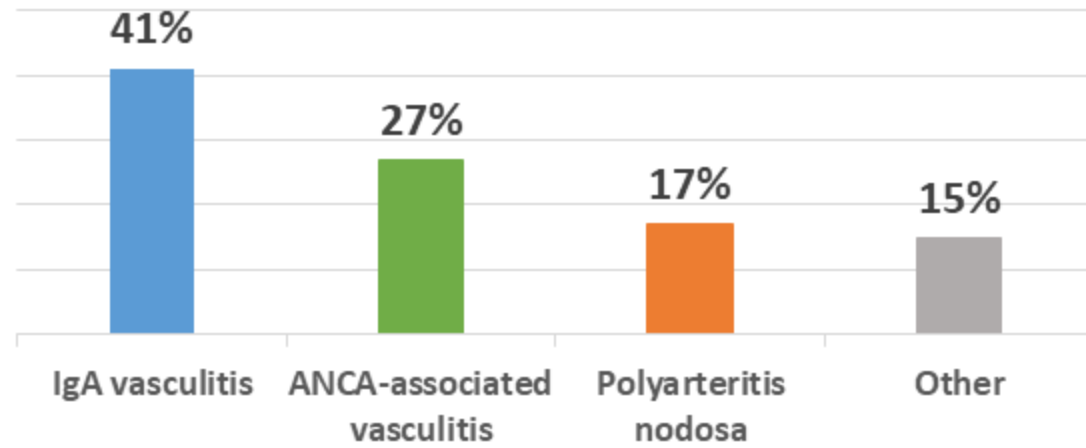
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- 435

Systemic Vasculitis



Factors associated with complicated outcome

PAN subtype	Increased leukocytes
Performance status	Low hemoglobin
Use of morphine	Increased CRP
Abdominal guarding	
Ileus	
Melena	

Predicted probability

Intensive care unit admission
Emergency surgical procedure
Death

