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Quantifying physician's bias to terminate resuscitation. The TERMINATOR Study

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22

23

24

Abstract

25 Context

26 Deciding on "termination of resuscitation" (TOR) is a dilemma for any physician facing cardiac arrest.

27 Due to the lack of evidence-based criteria and scarcity of the existing guidelines, crucial arbitration to

28 interrupt resuscitation remains at the practitioner's discretion.

29 Aim

30 Evaluate with a quantitative method the existence of a physician internal bias to terminate resuscitation.

31 Method

32 We extracted data concerning OHCA managed between January 2013 and September 2021 from the

33 RéAC registry. We conducted a statistical analysis using generalized linear mixed models to model the

34 binary TOR decision. Utstein data were used as fixed effect terms and a random effect term to model

35 physicians personal bias towards TOR.

36 Results

37 5,144 OHCA involving 173 physicians were included. The cohort's average age was 69 (SD 18) and

38 was composed of 62% of women. Median no-flow and low-flow times were respectively 6 (IQR [0,12])

39 and 18 (IQR [10, 26]) minutes. Our analysis showed a significant ($p < 0.001$) physician effect on TOR

40 decision.

41 Odds ratio for the "doctor effect" was 2.48 [2.13-2.94] for a doctor one SD above the mean, lower than

42 that of dependency for activities of daily living (41.18 [24.69-65.50]), an age of more than 85 years

43 (38.60 [28.67-51.08]), but higher than that of oncologic, cardiovascular, respiratory disease or no-flow

44 duration between 10 to 20 minutes (1.60 [1.26-2.00]).

45 Conclusions

46 We demonstrate the existence of individual physician biases in their decision about TOR. The impact of

47 this bias is greater than that of a no-flow duration lasting ten to twenty minutes. Our results plead in

48 favor developing tools and guidelines to guide physicians in their decision.

50

51 **Introduction**

52 Deciding on “termination of resuscitation” (TOR) is a frequent dilemma for any physician whose activity
53 includes cardiac arrests management. They can be brought to the point of interrupting basic life support
54 (BLS) when the latter have been initiated by bystanders or first aiders. They can also choose to stop
55 advanced life support (ALS) when it fails to elicit a return of spontaneous circulation (ROSC). Lastly,
56 they can be brought to stop post-resuscitation care when anoxic sequelae post resuscitation prohibits
57 satisfactory clinical outcome. Few guidelines exists concerning TOR.^{1,2} In the setting of BLS for
58 emergency medical technician, recommendations suggest that they terminate resuscitation based on
59 the joint absence of witness, shockable rhythm and ROSC. In France, such decisions are constantly
60 taken by physicians with the possibility to start an ALS procedure. Thus, a cardiac arrest without
61 witness, a no-flow time of more than 5 minutes (time between cardiac arrest and first chest
62 compressions), a low-flow time (duration of chest compressions before ROSC or death) of more than
63 20 minutes, all known to be associated to a weak prognosis, tend to lead towards TOR. Conversely, a
64 young age, an initial shockable rhythm, both linked to a better outcome, prompts to pursue life-
65 supporting care.³ Nevertheless, the final TOR decision remains above all at the physician's discretion.
66 Any such decision remains medically and ethically difficult.⁴⁻⁶, and knowing which factor contribute to
67 cardiac arrest prognosis is of primary interest. One may assume that physicians integrate, consciously
68 or unconsciously, factors based on culture, experience, or training. Environmental factors, such as the
69 presence of family members for instance, may influence decision-making.⁷⁻⁹ The focus of this study is
70 to test the hypothesis that some physicians have a greater or lower intrinsic tendency to terminate
71 resuscitation than average regardless of clinical factors, tendency that we term the “doctor effect”, and
72 quantify it using Generalized Linear Mixed Models.

73

74 **Methods**

75 In France, medical emergencies are managed by the SAMU–Emergency Medical System (SAMU-
76 EMS). This organization relies on a medically assessed dispatch system and medical pre-hospital
77 care.¹⁰ The national medical emergency telephone number, 15, connects the caller to an Emergency
78 Physician. The latter has the possibility, if necessary, as in case of cardiac arrest to send a Mobile
79 Intensive Care Unit (SAMU-MICU) with a team comprised of an emergency physician, a nurse and an
80 ambulance driver. If another emergency phone number is called (such as 112, European emergency

81 call number), it is managed similarly and in case of cardiac arrest, a SAMU-MICU is sent on site. A team
82 is sent every time an extra-hospital cardiac arrest (OHCA) is suspected. This organization is consistent
83 within the whole country of France.

84

85 [Setting](#)

86 The Seine-Saint-Denis is an urban department counting 1.6 million inhabitants. It is the north-eastern
87 suburban areas of Paris, which it borders, and covers 236 km². SAMU-EMS manages almost
88 225.000 patients per year. Medical intervention teams are headquartered within five hospitals over the
89 department.

90

91 [Data collection](#)

92 All patients with out-of-hospital cardiac arrest managed by a SAMU-MICU team are systematically
93 included in the French nationwide RéAC (Cardiac Arrest Electronic Registry) registry. The detailed
94 registry filling methodology has been previously published.¹¹ All cardiac arrests were included,
95 regardless of aetiology and the way they were managed by the SAMU-MICU team, i.e., with advanced
96 life support or not. Recorded parameters encompass many fields of cardiac arrest management:
97 patient's demographic information, circumstances of occurrence of cardiac arrest, medical
98 management, delays, and evolution, including Utstein universal-style guidelines. All parameters were
99 prospectively recorded on a dedicated case report form (CRF) by the emergency physician. In each
100 SAMU-MICU, an emergency physician oversees the completeness of inclusions and data collection,
101 reviewing the entirety of intervention reports allowing to reach data exhaustivity. All the data was
102 reported in the national RéAC databank. SAMU-EMS departments of Seine-Saint-Denis have been
103 taking part in the RéAC registry since January 2013.

104

105 [Data selection](#)

106 We first selected several criteria identified in the literature as being associated with cardiac arrest
107 outcome and consequently considered to contribute to the emergency physician's TOR decision.^{12,13}
108 For a factor to be of interest for our study, it must have been immediately or quickly available to the
109 physician when arriving at the site of the OHCA. Indeed, the decision of TOR must be made quickly
110 upon arrival of the emergency physician, possibly before obtaining the detailed patient's history.
111 Selected variables were either related to the patient: age, gender, dependency for activities of daily
112 living, cardiac medical history, diabetes, oncologic or other medical history; to the cardiac arrest: initial
113 rhythm (shockable or non-shockable rhythms), duration of no-flow, duration of low-flow and return to

114 spontaneous circulation before physician arrival or to the environment: the presence of a witness.
115 Lastly, the physician's identity was known for each cardiac arrest and replaced by a numeric identifier to
116 preserve anonymity.
117 Patients with cadaveric rigidity were excluded from the analysis as well as patients with trauma cardiac
118 arrests as, for the latter, prognostic factors are known to be different from those of medical cardiac
119 arrest.¹⁴ All this information concerning OHCA in Seine-Saint-Denis managed between 01/01/2013 and
120 14/09/2021 was extracted from the RéAC registry.

121

122 [Endpoints](#)

123 The endpoint was to ascertain the existence of physician's individual bias in terminating resuscitation,
124 aka "doctor effect", and quantify its importance when compared to other factors influencing TOR
125 decision.

126

127 [Analysis](#)

128 To assess the existence of a statistically significant "doctor effect", we performed a likelihood ratio test
129 between a Generalized Linear Model (GLM) (logistic regression model) and a Generalized Linear Mixed
130 Model (GLMM) differing from the GLM only by the addition of the "doctor effect" as a random effect
131 parametrized by σ_{DE} . Detailed explanations about this methodology are given in appendix 1. To validate
132 the applicability and validity of our logistic regression and GLMM models, we conducted three
133 complementary analyses (detailed results and analysis in [appendix 2](#)), in accordance with good practice
134 when using these types of models¹⁵ : fixed variable independence; normal distribution of the random
135 effect ("doctor effect") and independence of the random effect from other variables (exogeneity). Since
136 linearity assumptions could not be satisfied, continuous variables (no-flow, low-flow and age) were
137 categorized. Estimates for a fully linear model and for a model including quadratic terms for continuous
138 variables are reported in Appendix 3.

139 To further strengthen our conclusions, we conducted some sensitivity analysis. We replicated a similar
140 statistical procedure, firstly excluding OHCA attended by physicians who had taken care of less than
141 three OHCA in our database ([appendix 4](#)), and secondly excluding the gender factor, which is the most
142 debatable clinically speaking ([appendix 5](#)).

143 We evaluated our choice of covariates, by comparison of AIC and pseudo-R² (using the method from
144 Nakagawa et al.¹⁶), between the GLMM of the main analysis and GLMMs excluding some covariates
145 ([appendix 5](#)).

146 To evaluate the contribution of each factor (including the “doctor effect”), we calculated their odds-ratio,
147 For the random effect we report normalized odds-ratios. Odds-ratios for fixed effects were computed
148 directly by exponentiating beta coefficients. For the random effect, the normalized odds-ratio was
149 calculated by exponentiating the standard deviation of the random effect (i.e. the typical magnitude of
150 the “doctor effect” for a doctor one SD above average in his tendency to terminate resuscitation). By
151 construction, the random effect is symmetric and models both physicians with higher tendency than
152 average (OR>1) and physicians with tendency lower than average (OR<1) to terminate resuscitation.
153 We thus also displayed the odds-ratio of the doctor effect for a physician one SD beneath the mean.
154 95% confidence intervals for all factors were computed using a semi parametric bootstrap.

155

156 All analyses were conducted using R v4.1.1 and lme4 1.1-27.1, and the code is available in appendix 6.
157 Quantitative variables are expressed as medians (IQR) and qualitative as proportions (%).

158

159 [Regulatory framework - Ethics](#)

160 RéAC is a national registry.¹⁷ It has been recorded at the French advisory committee on information
161 processing in health research (CCTIRS) and in the French national Data protection commission
162 (CNIL 910946). Under French law, this registry has been approved as a medical assessment requiring
163 no specific patient consent, and no specific authorization was required to perform this analysis on the
164 database. No fund supported this study.

165 **Results**

166 [Population](#)

167 During the study observation time, 7378 patients with OHCA were included. The cause of cardiac arrest
168 was traumatic in 1046 (14%) of cases, and 977 (13%) were in cadaveric rigidity at SAMU-MICU arrival.
169 These patients were excluded from the analysis. On the 5355 patients left, gender (N=3; 0.05%), no-
170 flow or low-flow duration (N=147; 3%), initial rhythm (N=40; 0.7%), or doctor identity (N=21; 0.4%) were
171 missing, and the corresponding patients were excluded from the analysis. Finally, 5144 patients were
172 included in the study (Figure 1).

173

174 The included patients were managed by 173 different physicians. This corresponded to a median of 14
175 (IQR [2,37]) OHCA per physician. Among those patients, the TOR decision has been taken 1.851 (35%)
176 times and advanced life support has been carried on 3.293 (65%) times. Patients’ characteristics—
177 according to ALS or TOR decisions—are reported in Table 1.

178

179 [Endpoint](#)

180 Performing a likelihood ratio test between our GLMM and logistic regression model, we found that the
181 magnitude of the “doctor effect”, σ_{DE} , was significantly different from 0 ($p < 0.001$).

182 Estimated odds-ratios and 95% confidence intervals for all factors in the GLMM are reported in Table 2
183 and illustrated in Figure 2. The odds-ratio for each factor explicative of TOR decision was, in decreasing
184 order of importance: 41.18 [24.69-65.50] concerning dependency for activities of daily living, 38.60
185 [28.67-51.08] for an age superior to 85 years, 0.05 [0.00-0.12] for ROSC, 10.02 [7.85-12.58] for an age
186 between 75 and 85 years, 0.19 [0.12-0.28] for low-flow duration of more than 40 minutes, 4.64 [3.16-
187 6.78] for non-shockable initial rhythm, 3.62 [2.52-5.03] for no-flow duration of more than 20 minutes,
188 2.87 [2.23-3.61] for an age between 65 to 75 years, 0.35 [0.29-0.42] for witness presence, 0.39 [0.31-
189 0.48] for low-flow duration between 20 to 40 minutes, 2.48 [2.13-2.94] for the “doctor effect” considering
190 a doctor one SD above the mean, or 0.40 [0.34-0.47] considering a doctor one SD beneath the mean,
191 2.17 [1.82-2.60] for oncologic or other relevant disease, 0.46 [0.37-0.57] for low-flow duration between
192 10 to 20 minutes, 1.61 [1.28-2.07] for no-flow duration between 5 to 10 minutes, 1.60 [1.26-2.00] for no-
193 flow duration between 10 to 20 minutes, 1.31 [1.10-1.56] for male gender, 1.23 [0.98-1.52] for
194 respiratory disease, 0.81 [0.64-1.00] for diabetes, 0.86 [0.71-1.04] for cardiovascular disease and 1.11
195 [0.83-1.44] for no-flow duration between 1 to 5 minutes.

196 [Discussion](#)

197 [Interpretation](#)

198 The existence of a different propensity to terminate resuscitation among physicians has been suspected
199 but it’s the first time that it is evaluated using a quantitative strategy. Our study confirms, using a robust
200 methodology, the existence of such a “doctor effect”, and measures its influence concerning TOR
201 decisions. Before going further in the interpretation, a word of caution is to be added upon comparing
202 odds-ratios between them: random effects was normalized to one SD, thus its reported normalized
203 odds-ratio only account for a portion of its possible importance in the TOR decision. On the contrary, for
204 binary and categorical factors, reported odds-ratios represent the full spectrum of their potential effect.
205 This can only contribute to minimize the importance of the “doctor effect” when compared to binary
206 variables, allowing conclusions to be drawn when comparing against factors of lesser influence (OR
207 closer to 1). Interestingly, the results revealed that the OR of the "doctor effect" was higher than that for
208 a no-flow period lasting ten to twenty minutes or the presence of significant comorbidities. Its influence

209 was only second to the presence of a witness, age, initial cardiac rhythm, ROSC, and dependency for
210 activities of daily living.

211 Thus, physicians facing critical situations such as OHCA, are themselves important decisional factors
212 concerning the termination or continuation of resuscitation. This heterogeneity between doctors is likely
213 to be multifactorial. These decisions, made on site with few parameters available, make it hard to
214 evaluate the prognosis of patients, and the constraints of emergency reinforce the importance of bias
215 and emotions.^{7,18} Knowledge importance has also been studied in OHCA through initial formation,
216 without having much impact on prognosis evaluation or survival on most studies, some finding with a
217 low level of proof a little benefit on mortality.¹⁹⁻²¹ Influence of emotions in clinical decisions, factors such
218 as age or gender, ethics, culture, and even religion of doctors, could explain to some extent the
219 differences observed in our study.^{7,8,22-24} Family presence during the process of resuscitation has been
220 studied and shows different results between countries, reinforcing the possibilities of a cultural
221 implication in the decision-making process of clinicians.⁹

222

223 [Strengths of this study](#)

224 This study, using the RéAC register, is multicentric, with a quantitative approach, and finds its strengths
225 primarily in its robust and innovative statistical methodology and its good statistical power, with
226 173 different physicians involved and 5144 OHCA included. The automatic inclusion of every cardiac
227 arrest in the register limits the recruitment bias, and the multiple quality controls ensures a good data
228 reliability and exhaustivity. All analysis of validity and performance converge towards an appropriate
229 model ([appendix 2](#)). Other sub-analysis concerning points of discussions (excluding doctors with few
230 OHCA or excluding gender as a determining factor of TOR) showed no big difference concerning our
231 endpoint results (see appendixes 4 and 5), further validating the results. The odds-ratio of the “doctor
232 effect” was consistent in all the variations of the model that we tested (see appendixes 2-4-5) showing
233 resilience to variables choices.

234

235 [Limitations](#)

236 Study limits, beyond limitations intrinsic to those of a linear model, include the choice of variables that
237 are not fully independent. However, one study has shown the robustness of GLMMs to perturbations
238 due to correlations between variables²⁵ and the physician’s identity used to study the doctor effect is
239 most unlikely to be correlated to any of the patient’s characteristics. Another issue is the risk of
240 oversimplifying complex situations through a few factors, that are in themselves subject to human
241 interpretation. For instance, reporting “dependency for activities of daily living” may be interpreted

242 differently among physicians. Such effects could have been modelled by random slopes terms in the
243 GLMM framework, modelling different interpretation of each factor by different physician. However,
244 adding such terms entails adding a very large number of parameters, a number not realistic despite our
245 sample size and GLMMs statistical efficiency. Also, our model implicitly considers that every physician
246 knows all factors included in the model when taking it's TOR decision, which can obviously be false, no-
247 flow being a good example of a regularly unknown variable in an OHCA without witness, and this effect
248 is limited only by the size of our sample. This effect could also explain the relatively low importance of
249 some pre-existing co-morbidities in our model. Finally, our results suggest that longer low-flow
250 decreases odds of TOR, although it is known to correlate with poor prognosis.²⁶ We hypothesize that
251 this could be explained by confounding factors missing from the RéAC database, intricate interactions
252 among existing covariates or the social challenge clinicians face in ending resuscitation after non-
253 medical personnel performed CPR.

254

255 [Consequence and perspective](#)

256 The existence of this “doctor effect” raises legitimate questions. Studying the reasons of this
257 heterogeneity between caregivers' attitude should also help reduce the gap we observe today. Making a
258 TOR decision implies two aspects, technical and ethical. As of now, clinicians are left in the dark
259 concerning these two dimensions, without ethical guidelines on acceptable risks or efficient tools for
260 technical aspects. On the technical side, prognosis evaluation remains a challenge, given the limited
261 amount of information available on an OHCA scene. Part of the difference observed between doctors
262 could be the result of this difficulty for practitioners to evaluate the prognosis of the patients.²⁷
263 Implementing TOR rules can be a partial solution to this problem. Different TOR rules have been
264 evaluated on the basis of specificity and sensibility to survival.^{1,27-29} Those studies have shown a good
265 specificity for mortality but cannot guarantee not to leave potential survivors behind.³⁰ What's more,
266 interpretation of sensibility on mortality is tough, since application of TOR rules has a direct impact on
267 mortality, introducing a bias in mortality count.^{31,32} This bias is found in many studies or meta-
268 analysis.^{27,29} The efficacy of the implementation of TOR rules on resuscitation frequency has also been
269 evaluated, for medical as well as paramedical support in OHCA, lowering the number of resuscitation in
270 some place and increasing in others, depending on local policies in place before these
271 experimentations.^{28,29,33} Another interesting proposition is to make prognosis scores to guide
272 practitioners', instead of using rigid recommendation or rules, leaving the human aspect of the decision
273 in the hand of the doctor. Such scores exist but their effect have not been evaluated yet.^{34,35}

274 On the ethical aspect, the question is sensitive, but leaving the clinician settle it in those complex
275 situations without guidelines seems also questionable, given the importance of personal beliefs and
276 feelings in such stressful situations. Of course, no guidelines can substitute the human aspect of the
277 delicate mediation of TOR, but general advice could help reducing the difference in medical support
278 between doctors based on ethical discussions held upstream of emergency. Even if evaluating the
279 importance of the effect necessary to change practice is a debate in itself, excessive resuscitation has
280 an important ethical and financial impact, that could be tremendously mitigated by using TOR decision
281 when appropriate before hospital admission.³⁶ Finally, perhaps the most interesting part of this study is
282 the usage of its reliable statistical methodology to measure the impact of physician's identity in a
283 medical decision. The proposed statistical method is general and could be applied to assess inter-
284 physician variability in any clinical decision, provided good quality data.

285 Conclusion

286 In this study, we demonstrate for the first time the existence of a "doctor effect," i.e. physician's internal
287 bias that influences TOR decisions in OHCA. The impact of this bias on our model is greater than that of
288 a no-flow duration lasting ten to twenty minutes or the presence of significant pre-existing co-morbidities
289 such as oncological, cardiovascular, or respiratory disease. While human judgment remains a part of
290 this mediation, improving the comprehension of this heterogeneity, exploring solutions such as
291 reinforcing ethical guidelines, and using prognosis tools, should be of interest to the medical community.

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294

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