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Letter to the Editor

Reply to: Prognostic value of signs of life in refractory out-of-hospital cardiac arrest



We thank Dr Patel et al. for their interest in our article entitled “Prognostic value of signs of life throughout cardiopulmonary resuscitation for refractory out-of-hospital cardiac arrest”, recently published in *Resuscitation*.¹ We would like to bring some additional insights regarding the issues they raised in their letter.

First, Patel et al. question the consistency of advanced life support (ALS) guidelines over the recruitment period, which spanned from 2009 to 2017 across the three primary cohort studies. Actually, French guidelines for extracorporeal cardiopulmonary resuscitation (ECPR) did not change over the study period.² Although compliance with current ALS guidelines was advocated, physicians on scene could

adjust therapies according to individual characteristics or local clinical practices in these observational studies.

Second, Patel et al. might have misunderstood the patterns of missing values for any sign of life in our study. Basically, this variable was a composite of gasping, pupillary light reaction, and increased level of consciousness. Any sign of life was missing if any component yielded missing value while the other were coded as « no ». As shown in [Table 1](#), there were seven patterns, totaling 54 individuals, with missing values for any sign of life (i.e., pattern 3, 7, 9, 19, 21, 25, 27). Hence, the denominator for computing the prevalence of any sign of life was 380 (i.e., 434–54).

Table 1 – Patterns of missing values for any sign of life (n = 434).

Pattern	Gasping	Pupillary light reaction	Increased level of consciousness	Any sign of life	No. individuals
1	No	No	No	No	150
2	No	No	Yes	Yes	0
3	No	No	Missing	Missing	0
4	No	Yes	No	Yes	68
5	No	Yes	Yes	Yes	10
6	No	Yes	Missing	Yes	4
7	No	Missing	No	Missing	4
8	No	Missing	Yes	Yes	11
9	No	Missing	Missing	Missing	48
10	Yes	No	No	Yes	12
11	Yes	No	Yes	Yes	1
12	Yes	No	Missing	Yes	3
13	Yes	Yes	No	Yes	51
14	Yes	Yes	Yes	Yes	20
15	Yes	Yes	Missing	Yes	1
16	Yes	Missing	No	Yes	39
17	Yes	Missing	Yes	Yes	7
18	Yes	Missing	Missing	Yes	2
19	Missing	No	No	Missing	2
20	Missing	No	Yes	Yes	0
21	Missing	No	Missing	Missing	0
22	Missing	Yes	No	Yes	1
23	Missing	Yes	Yes	Yes	0
24	Missing	Yes	Missing	Yes	0
25	Missing	Missing	No	Missing	0
26	Missing	Missing	Yes	Yes	0
27	Missing	Missing	Missing	Missing	0
Missing values, n	3	111	58	54	...
Denominator, n	431	323	376	380	...

The intention-to-treat approach is relevant for randomized controlled trials but may not be suitable for observational studies. Indeed, the occurrence of signs of life was not based on random assignment in our observational study and its prognostic significance is unlikely to be studied by randomized controlled trials. Yet, we performed multiple imputations of missing values in order to circumvent the problem of missing data.

Third, we concur with Patel et al. that ECPR might benefit a limited number of patients. Because the receipt of ECPR was an inclusion criterion across the three primary studies, we could not determine accurately which percentages of OHCA individuals experienced refractory cardiac arrest and showed signs of life throughout cardiopulmonary resuscitation. Importantly, outcomes for ECPR recipients with refractory cardiac arrest relate with many factors including initial cardiac rhythm, cardiopulmonary resuscitation quality, delay in ECPR implementation, ischaemia-reperfusion injuries and signs of life.^{3,4} Cost-effectiveness analysis of ECPR need to account for the fact that most patients are young (mean 49 ± 13 years) and 63/69 (91%) survive with favorable neurologic function. Consistently, most recent guidelines consider ECPR as a rescue therapy for selected patients with cardiac arrest when conventional ALS measures are failing or in order to facilitate specific interventions.⁵

Conflict of interest

None of the other authors have any financial conflict of interest to disclose.

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