Received: 1 September 2023 | Revised: 20 November 2023 | Accepted: 21 December 2023

DOI: 10.1111/aas.14374

RESEARCH ARTICLE

acta Anaesthesiologica Scandinavica

Transthoracic impedance variability to assess quality of chest compression in out-of-hospital cardiac arrest

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Funding information
Thelma Zoéga Foundation; Region Skåne; Stig Ragna Gorthon's Foundation; Horizon 2020 Framework Programme, Grant/Award Number: 733381

Abstract

Background: Chest compression is a lifesaving intervention in out-of-hospital cardiac arrest (OHCA), but the optimal metrics to assess its quality have yet to be identified. The objective of this study was to investigate whether a new parameter, that is, the variability of the chest compression-generated transthoracic impedance (TTI), namely Imp_{CC}, which measures the consistency of the chest compression maneuver, relates to resuscitation outcome.

Methods: This multicenter observational, retrospective study included OHCAs with shockable rhythm. Imp_{CC} variability was evaluated with the power spectral density analysis of the TTI. Multivariate regression model was used to examine the impact of Imp_{CC} variability on defibrillation success. Secondary outcome measures were return of spontaneous circulation and survival.

Results: Among 835 treated OHCAs, 680 met inclusion criteria and 565 matched long-term outcomes. Imp_{CC} was significantly higher in patients with unsuccessful defibrillation compared to those with successful defibrillation ($p = .0002$). Lower Imp_{CC} variability was associated with successful defibrillation with an odds ratio (OR) of 0.993 (95% confidence interval [95% CI], 0.989–0.998, $p = .003$), while the standard chest compression fraction (CCF) was not associated (OR 1.008 [95 % CI, 0.992–1.026, $p = .33$]). Neither Imp_{CC} nor CCF was associated with long-term outcomes.

Conclusions: In this population, consistency of chest compression maneuver, measured by variability in TTI, was an independent predictor of defibrillation outcome. Imp_{CC} may be a useful novel metrics for improving quality of care in OHCA.

KEYWORDS
cardiopulmonary resuscitation, chest compression fraction, outcome, transthoracic impedance, variability

Editorial Comment

Consistent high-quality chest compression is known to increase the likelihood of good outcome for cases of cardiac arrest. In this study cohort, transthoracic impedance was recorded during

resuscitation and chest compressions, where there was a shockable rhythm. Lower variability in chest compression effect, as shown by chest impedance measures, was associated with better defibrillation response, confirming the importance of working to optimize chest compression quality in practice.

1 | INTRODUCTION

Cardiopulmonary resuscitation (CPR) is a lifesaving intervention in patients with cardiac arrest. Providing high-quality chest compression increases the likelihood of successful resuscitation and improves survival, while heterogeneity in CPR quality may contribute to variable survival rates.[1–3]

Minimally interrupted chest compression delivered with adequate depth and rate represents a comprehensive approach to ensure high-quality CPR. Although the individual impact of these CPR metric components is difficult to evaluate, chest compression fraction (CCF), that is, the time devoted to perform chest compression over the entire duration of the resuscitation, has been commonly used as a general parameter to describe the overall CPR quality in out-of-hospital cardiac arrest (OHCA).[4–6] Current recommendations on quality of CPR are; however, based on a very low and heterogenous level of evidence, such that the identification of the optimal chest compression metrics to guide CPR is still a knowledge gap requiring further research.[4]

Our group has recently investigated the quality and consistency of manual versus mechanical chest compression during ambulance transport with ongoing CPR in a porcine model of cardiac arrest.[7] Of interest, was the greater hemodynamic support and systemic perfusion generated by mechanical compression in comparison to manual compression during transport, despite the equally high CCF in both interventions, that is, >90%. Thus, in that study, CCF role in identifying the real CPR quality was limited.[7] In contrast, a new parameter assessing the consistency of chest compression through analysis of the variability of the chest compression-generated transthoracic impedance (Imp_{CC}), discriminated the quality of CPR. Indeed, deterioration of the manual compression consistency during transport has been effectively quantified by the higher Imp_{CC} variability.[7] Despite evidence from this animal study suggested the importance of chest compression quality consistency during CPR, no human studies have been conducted so far to corroborate this experimental finding.

Thus, the objective of the present multicenter retrospective cohort study was to investigate whether the analysis of Imp_{CC} variability could be used to assess chest compression quality and to estimate its association with defibrillation success and long-term outcomes in a cohort of patients with OHCA with shockable rhythm, in comparison with the traditional CCF. Differently from CCF, Imp_{CC} variability could be a new general CPR metric parameter to measure the consistency and harmony of chest compression maneuvers. Indeed, reducing the variability in how chest compression is executed, might enhance the quality of CPR and ultimately improve likelihood of termination of ventricular fibrillation (VF) and survival.

2 | MATERIALS AND METHODS

This was a multicenter observational, retrospective cohort study conducted according to the Declaration of Helsinki and the Italian Guidelines of Good Clinical Practice and Data Protection Code. The study protocol was approved by the institutional review board of the coordinating center, San Gerardo University Hospital, Lombardy, Italy. The ECG traces used for this study were already collected for an earlier investigation on VF waveform analysis to predict defibrillation outcome.[8]

The institutional review board waived the requirement of informed consent, in accordance with government laws regulating the use of human clinical data (legislative decrees 196/2003, article 5, paragraph 4, and article 110, paragraph 1), as follows: (1) The data were already collected for administrative and statistical reasons by the National Health System; (2) the study was a retrospective observational analysis with no foreseeable harm expected or changes in patients' treatment; (3) the waiver of consent did not adversely affect the rights and welfare of the patients; and (4) the data were used in accordance with national and regional laws regulating patients' confidentiality (legislative decrees 196/2003, regional law No. 9, July 18, 2006, and No. 7, February 5, 2010).

2.1 | Patient population and data sources

All cases of OHCA with a first recorded shockable rhythm (VF or pulseless ventricular tachycardia) by the Physio Control automated external defibrillators (AEDs, Stryker, WA, USA) between 2008 and 2010 in the Lombardy Region, Italy, were eligible. Patients who received <1 min of digitally recorded CPR, or with a transthoracic impedance (TTI) waveform recorded incompletely or halted due to technical problems were excluded from the study. TTI waveforms recorded during prehospital CPR in three city areas in the Lombardy region of Italy (Milan, Monza, and Varese) were used for the study. CPR was performed by basic life support and defibrillation (BLSD) crews with a 30:2 compression: ventilation ratio with no advanced airway. The BLSD crew was composed by volunteer rescuers trained to recognize cardiac arrest and start BLS maneuvers and defibrillation, while an advanced vehicle with a physician on board was sent to the scene.[9] TTI and ECG[AQ: Please define (ECG) in the first occurrence if necessary.] waveforms were prospectively collected from the emergency medical services (EMS) of each area for administrative and statistical reasons. EMS groups were coordinated by the regional directing center, Agenzia Regionale Emergenza Urgenza (AREU), located in Milan, and all used the same electronic data management system and data validation software EMMA (Emergency Management, Beta 80 Group, Milan, Italy).

All TTI and ECG waveforms were stored on CODE-STAT 9.0 (Physio-Control, Stryker, WA, USA).

Each TTI waveform included in the study and analyzed was then matched to the proper record in EMMA, which collects information on the prehospital events and patients' identification data. More specifically, the prehospital data collected in EMMA used in this study were the EMS arrival time and the cause of EMS alert. Individual patients' identification data were used instead to retrieve additional information for each patient from the administrative healthcare databases. Data were subsequently anonymized. A regional data warehouse that organized the administrative databases of the public-funded National Healthcare System (DENALI), was used to collect data regarding vital status (survival), hospital discharge, and daily pharmaceutical and outpatient claims in the general population living in Lombardy.[8,10] Patients' data were automatically validated and updated annually by an in-house software for regional epidemiological and research purposes. The linkage between EMMA and DENALI used a probabilistic approach to the data for patients' identification.[11] The exact match was found for 565 patients (83%) of the total of 680 TTI waveforms that were analyzed.

2.2 | Measurements

The presence of chest compression was measured by changes in TTI recorded from the two defibrillator pads.[12] TTI and ECG waveforms stored on CODE-STAT 9.0 (Physio-Control, Stryker, WA, USA) were exported as comma-separated values (.csv) and converted to a common LabChart file format (LabChart 8.0, ADInstruments, UK) for the analysis of the Imp_{CC} variability (Figures 1 and S1). TTI signal from the last 5 min of the resuscitation maneuvers, that is, chest compression performed and recorded by the AED, was converted from a time to a frequency domain by fast Fourier transformation (FFT). The power spectral density analysis of the TTI signal, excluding pauses for ventilations (in order to let Imp_{CC} variability reflecting only chest compression maneuvers), was then calculated using the specific preset algorithm of LabChart 8.0 algorithm, with the following sets: range of frequencies 0 (lower)–5 (upper) Hz; FFT size 1024. Imp_{CC} variability was quantified as a single overall Total Power (mOhms^2) value for the 5-min interval (Figure S2).[7] Indeed, the total power of spectral density analysis is mathematically equivalent to a variance (based on Parseval's theorem).

CCF was calculated using the CODE-STAT 9.0 CPR quality assessment tool (Physio-Control, Stryker, WA, USA), which uses the information derived from the TTI to measure the ratio of the time devoted to chest compressions over the entire duration of resuscitation maneuvers. CCF was calculated for the same last 5-min intervals of the resuscitation maneuvers used for the calculation of the Imp_{CC} variability. Appropriateness of automatically detected chest compressions by CODE-STAT was reviewed by two investigators and if needed corrected by manual annotations. CCF was categorized into three groups (CCF < 60%, 60%–80%, >80%) based on the 2021 European Resuscitation Council (ERC) recommendations which defined high-quality chest compression as compressions with a CCF of at least 60%.[1] Imp_{CC} variability was categorized into quartiles to explore the rate of defibrillation success.

2.3 | Study endpoints

The primary endpoint was the association between CCF and Imp_{CC} variability with the last defibrillation success (i.e., when attempted during or at the end of the 5-min chest compression interval analyzed), defined according to the established criteria: restoration of an organized rhythm with heart rate ≥ 40 bpm within 60 s after defibrillation. Whereas defibrillation failure was defined as the presence of an unorganized rhythm including VF, ventricular tachycardia, asystole, or low heart rate ≤40 bpm following defibrillation.[8,13]

Secondary endpoints included the association between CCF and Imp_{CC} variability with the following long-term outcomes: sustained return of spontaneous circulation (ROSC), corresponding to survival to hospital admission following cardiac arrest, survival to hospital discharge, 6-month and 1-year survival.

2.4 | Statistical analysis

Continuous and categorical data were expressed as mean ± SD or median with first and third quartiles and frequency (percentage), respectively.

Normal distribution of chest compression quality parameters (CCF and Imp_{CC} variability) was investigated. Comparisons between median values of chest compression quality parameters for defibrillation success were performed with Mann–Whitney test. Chi-square test was used for categorical data. Logistic regression was used to investigate the association between population and cardiac arrest characteristics and the defibrillation success, sustained ROSC, and survival at hospital discharge. Unadjusted and adjusted odds ratios, with the corresponding 95% confidence interval (95% CI), were reported. All significant variables in the univariate analysis were included in the multivariate regression model using a stepwise model selection. Finally, the discriminatory ability of CCF and Imp_{CC} variability was measured as area under the curve (AUC) with the use of defibrillation success as outcome. AUC with 95% CI and p-values for difference from chance (AUC $=$ 0.5) were reported. Differences among AUCs of the different VF parameters were tested assuming the mathematical equivalence of the AUC to the Mann–Whitney U-statistic.

3 | RESULTS

3.1 | Study population

Of the 835 OHCA patients with a presenting shockable rhythm and TTI waveforms recorded by the AEDs, 680 had adequate data

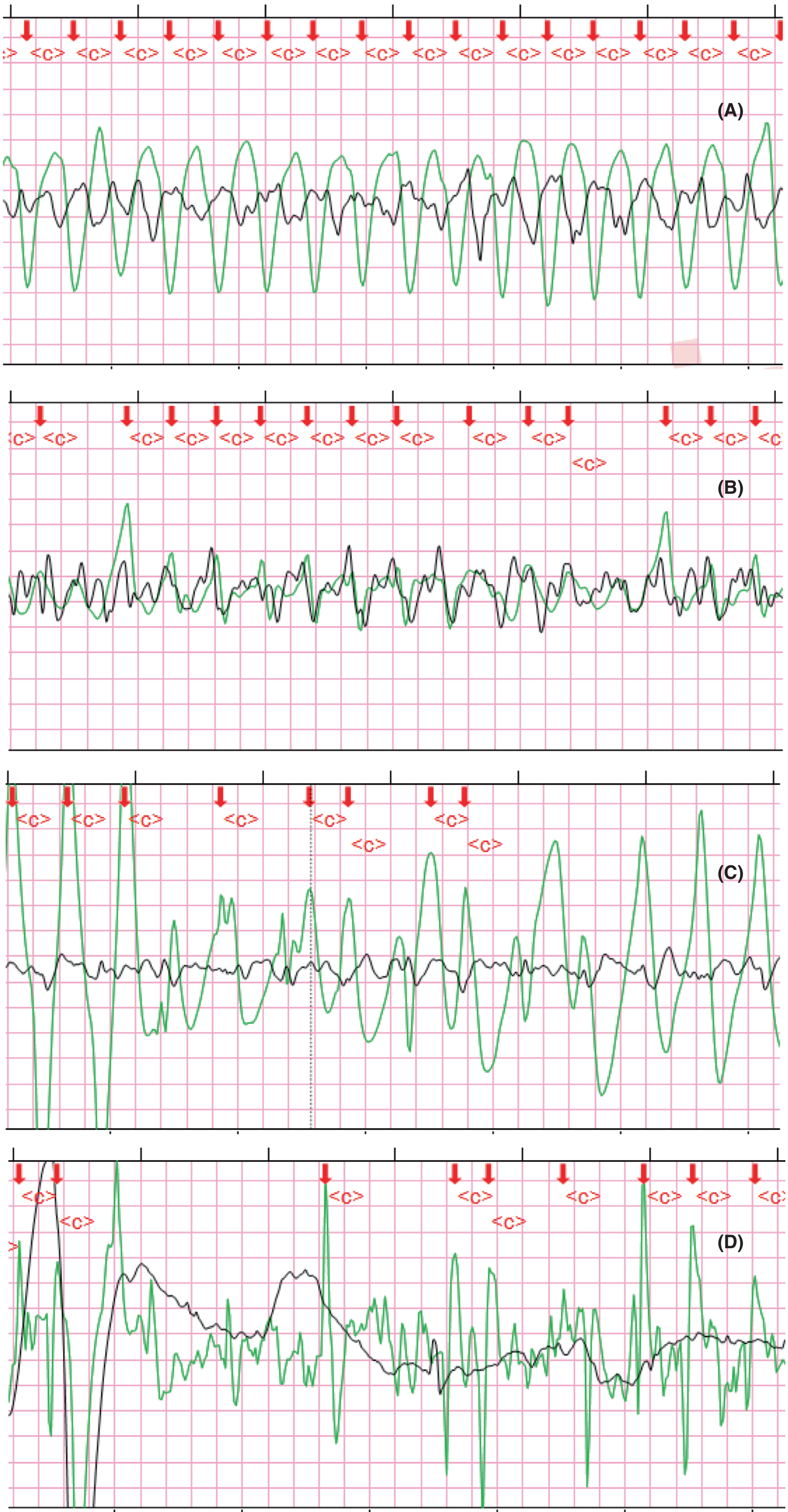

FIGURE 1 Transthoracic impedance (green line) representative tracings for (A) consistent chest compression (CC) with low thoracic impedance (Imp_{CC}) variability and for (B–D) variable CC quality accounting for a high Imp_{CC} variability.

TABLE 1 Population characteristics.

Variable	$n = 565$
Male sex, *n* (%)	396 (70.1)
Age, median (Q_1–Q_3)	71 (59–79)
Cause of EMS alert, *n* (%)	
Medical	528 (93.5)
Traumatic	29 (5.1)
Not declared	8 (1.4)
CPR intervention	
EMS arrival time, median (Q_1–Q_3)	8.3 (6.3–10.6)
No. of defibrillation attempts, median (Q_1–Q_3)	2 (1–3)
Chest compression fraction %, median (Q_1–Q_3)	66 (60–73)
Imp_{CC} variability mOhm^2, median (Q_1–Q_3)	2516 (498–5865)
Comorbidities, *n* (%)	
Previous myocardial infarction	75 (13.3)
Congestive heart failure	125 (22.1)
Peripheral vascular disease	50 (8.9)
Cerebrovascular disease	85 (15.0)
Chronic pulmonary disease	49 (8.7)
Diabetes mellitus	67 (11.9)
Liver disease	23 (4.1)
Renal disease	38 (6.7)
Cancer	50 (8.6)
Others	32 (5.7)
Not available	22 (3.9)
Number of concurrent comorbidities, *n* (%)	
0	284 (50.3)
1	84 (14.9)
2	73 (12.9)
3	56 (9.9)
≥4	46 (8.1)
Not available	22 (3.9)
Active drug treatment, *n* (%)	
Cardiac therapy	143 (25.3)
Antithrombotic drugs	197 (34.9)
Other antihypertensive drugs	20 (3.5)
β-blockers	115 (20.4)
Calcium channel blockers	104 (18.4)
Renin-angiotensin system antagonists	257 (45.5)
Cholesterol-lowering drugs	129 (22.8)
Selective β_2-adrenoreceptor agonists	8 (1.4)
Number of concurrent drug treatments, *n* (%)	
0	192 (34)
1	102 (18.1)
2	89 (15.8)
3	73 (12.9)
4	75 (13.3)
≥5	34 (6.0)

(Continues)

TABLE 1 (Continued)

Note: Data from 565 patients with known baseline characteristics and comorbidities from the DENALI regional database. Data are presented as count and proportion, or median and interquartile ranges (Q_1–Q_3) as appropriate.
Abbreviations: EMS, emergency medical services; Imp_{CC} variability, chest compression-generated thoracic impedance variability.

TABLE 2 Population outcomes.

Outcome, *n* (%)	$n = 565$
Sustained ROSC	174 (30.8)
Survival to hospital discharge	98 (17.3)
Six-month survival	82 (14.5)
One-year survival	77 (13.6)

Note: Data from 565 patients with known long-term outcomes from the DENALI regional database. Data are presented as count and proportion.
Abbreviation: ROSC, return of spontaneous circulation.

and were included in the study and analyzed (Figure S3). Cases with unavailable recordings ($n = 96$), artifacts ($n = 8$), or less than a minute of CPR data available ($n = 51$) were excluded. The median length of the CPR intervals analyzed (from the onset of chest compression to the last defibrillation attempt) in the cohort was 4.5 [2.3–7.2] min. Among the 680 patients with TTI, 674 had data on defibrillation success and represented the primary cohort. Baseline characteristics and long-term outcomes were available only for 565 patients and are summarized in Tables 1 and 2.

3.2 | Clinical outcomes

Data on defibrillation success were available in 674 patients. In 214 patients (31.8%), the defibrillation was successful. Sustained ROSC was achieved in 174 patients (30.8%) while survival to hospital discharge, 6-month and 1-year survival were 17.3%, 14.5%, and 13.6%, respectively (Table 2).

3.3 | Primary endpoint

Chest compression quality and defibrillation success are reported in Figure 2. The median value of CCF was 66% in patients with unsuccessful defibrillation and 68% in patients with successful defibrillation ($p = .017$, Figure 2A). Imp_{CC} variability was significantly higher in patients with unsuccessful defibrillation compared with patients with successful defibrillation ($p = .0002$, Figure 2B). Lower Imp_{CC} variability was associated with successful defibrillation, while CCF was not

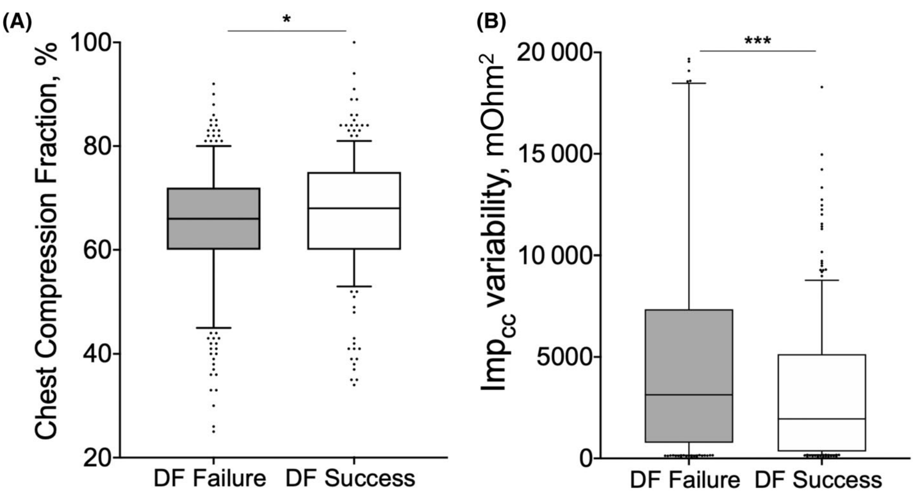

FIGURE 2 Chest compression quality and defibrillation (DF) success. Box plots of (A) chest compression fraction and (B) chest compression-generated thoracic impedance (Imp_{CC}) variability in patients with successful and unsuccessful defibrillations ($n = 674$ with transthoracic impedance tracings). Mann–Whitney test $^*p < .05$, $^{***}p < .001$ versus DF Failure.

TABLE 3 Logistic regression models for prediction of defibrillation success.

	Unadjusted univariate model			Adjusted multivariate model		
Covariate	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Shock number	0.755	0.642–0.887	.0006	0.75	0.636–0.885	.0006
Imp_{CC} variability,[a] mOhm^2	0.993	0.989–0.998	.0038	0.993	0.989–0.998	.0039
CCF, %	1.008	0.992–1.026	.3261	-	-	-
Age	0.998	0.985–1.01	.730	-	-	-
Gender (female vs. male)	1.381	0.935–2.04	.105	-	-	-
EMS arrival time[b]	0.984	0.93–1.04	.5751	-	-	-
Comorbidities						
Previous myocardial infarction	1.402	0.843–2.33	.193	-	-	-
Congestive heart failure	1.42	0.932–2.162	.1025	-	-	-
Peripheral vascular disease	1.56	0.858–2.837	.1448	-	-	-
Cerebrovascular disease	1.351	0.832–2.194	.2244	-	-	-
Chronic pulmonary disease	0.895	0.172–4.658	.8947	-	-	-
Diabetes mellitus	0.947	0.542–1.655	.8484	-	-	-
Liver disease	0.979	0.395–2.426	.9634	-	-	-
Renal disease	1.506	0.765–2.966	.2363	-	-	-
Cancer	1.42	0.777–2.595	.2537	-	-	-
Others	1.577	0.76–3.274	.2213	-	-	-
Number of concurrent comorbidities	1.135	0.994–1.295	.0607	-	-	-
Active drug treatment						
Cardiac therapy	1.165	0.77–1.76	.468	-	-	-
Antithrombotic drugs	1.351	0.93–1.97	.1179	-	-	-
Other antihypertensive drugs	1.035	0.39–2.22	.9453	-	-	-
β-blockers	1.006	0.64–1.58	.9784	-	-	-
Calcium channel blockers	0.702	0.43–1.15	.1609	-	-	-
Renin-angiotensin system antagonists	0.826	0.57–1.19	.3067	-	-	-
Cholesterol-lowering drugs	1.09	0.71–1.67	.6932	-	-	-
Selective β_2-adrenoreceptor agonists	1.35	0.32–5.72	.6835	-	-	-
Number of concurrent treatments	1.009	0.903–1.126	.8799	-	-	-

Note: Odds ratios (OR) and 95% confidence interval (CI) for defibrillation success in logistic regression models. Unadjusted univariate model and adjusted multivariate model with stepwise method. Data are available from 565 patients with known outcomes from the DENALI regional database.

Abbreviations: CCF, chest compression fraction; EMS, emergency medical services; Imp_{CC} variability, chest compression-generated thoracic impedance variability.

[a]Per 100 U increase in Imp_{CC} variability, mOhm^2.

[b]Per 1 min increase in EMS arrival time.

associated (Table 3). The AUC value for predicting defibrillation success was 0.58 (95% CI, 0.52–0.63, $p = .004$) for Imp_{CC} variability and 0.54 (95% CI, 0.48–0.59, $p = .19$) for CCF, with no differences between the two AUCs ($p = .33$). In a model combining together Imp_{CC} variability + CCF, the AUC did not increase compared with that of Imp_{CC} variability alone, that is, 0.56 (95% CI, 0.51–0.61, $p = .02$).

Defibrillation success by CCF and Imp_{CC} intervals is shown in Figure 3.

3.4 | Secondary endpoints

Neither CCF nor ImpCC variability was associated with sustained ROSC or survival to hospital discharge, as given in Tables 4 and 5.

4 | DISCUSSION

This multicenter observational, retrospective cohort study showed an association between chest compression-generated Imp_{CC} variability and defibrillation success in OHCAs with shockable rhythm. In the instance of successful defibrillation, the variability in Imp_{CC} was significantly lower compared with the unsuccessful ones. Imp_{CC} variability was an independent predictor of defibrillation success, indicating that the consistency in chest compression maneuvers enhances the probability of termination of VF in patients with OHCA. CCF, the commonly used parameter for CPR quality, although significantly higher in cases of defibrillation success, was not independently associated with defibrillation outcome. In this population, neither Imp_{CC} nor CCF was, however, associated with long-term outcomes.

This study showed for the first time the clinical application of the new parameter Imp_{CC} variability, obtained easily from the TTI recorded by every defibrillator through regular defibrillator pads. The results, therefore, provide a rationale for future prospective evaluation of the beneficial effect on outcome by implementing Imp_{CC} variability analysis in clinical practice, as well as in resuscitation training. Imp_{CC} variability represents a new general CPR metric parameter exploring the consistency in chest compression maneuver execution. Indeed, the quality of compression, derived from the TTI signal was suboptimal in the instance of failing defibrillations compared with successful ones. This might have likely been associated with the provision of chest compression with inconsistent depth and rate, that is, alternating chest compression with correct depth to shallower one, or with higher and lower rate or incomplete chest recoil, making chest compression less effective, or with chest compression performed with not correct movements, as previously described in our experimental study in the animal.[7] On the contrary, chest compression performed with consistent movements, depth, rate, and recoil, may allow for generation of a greater and constant blood flow and better tissue perfusion. Imp_{CC} does not provide feedback on compression depth or rate but on compression maneuver consistency, which can be qualitatively visualized by the TTI curve and quantitatively measured as variability. In this view, the use of this new CPR metric parameter, especially if used in conjunction with current accelerometers or feedback devices, which guide for optimal depth and rate, may further improve the quality of CPR and cardiac arrest outcome.

Current guidelines recommend a CCF target ≥60% to consider a CPR of high quality, as reported in several studies in which this set value allowed for the highest probability of resuscitation and survival.[4–6,14–17] In some instance, a high rate of sustained ROSC, survival to hospital discharge and survival with favorable neurological outcome was achieved only for CCFs >80% when the resuscitation maneuvers were longer than 20 min, while no differences were observed among different CCF categories for shorter CPR durations.[18] In contrast, indirect evidence from two recent randomized controlled trials failed to demonstrate a survival improvement with higher CCFs.[16,17] Similar results were also reported in three observational studies.[19–21] Altogether this evidence suggests that the definition of the optimal CPR quality measure is not unanimous and still particularly challenging. The physiological rationale for

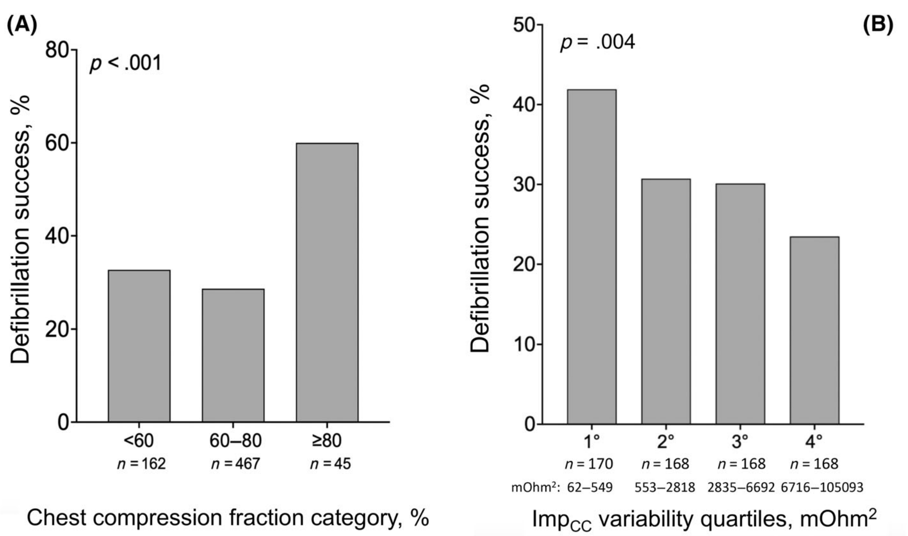

FIGURE 3 Defibrillation success for each category of chest compression fraction (A) and for each quartile of chest compression-generated thoracic impedance (ImpCC) variability (B, $n = 674$ with transthoracic impedance tracings). Chi-square test.

TABLE 4 Logistic regression models for prediction of sustained ROSC.

	Unadjusted univariate model			Adjusted multivariate model		
Covariate	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Age	0.963	0.951–0.976	<.0001	0.959	0.946–0.973	<.0001
EMS arrival time[a]	0.935	0.881–0.993	.0283	0.924	0.867–0.985	.0146
Shock number	0.797	0.683–0.93	.0039	0.73	0.618–0.862	.0002
Gender (female vs. male)	0.91	0.608–1.361	.6459	-	-	-
CCF, %	0.997	0.981–1.014	.7506	-	-	-
Imp_{CC} variability,[b] $mOhm^2$	0.999	0.996–1.001	.3536	-	-	-
Comorbidities						
Previous myocardial infarction	0.997	0.585–1.698	.9901	-	-	-
Congestive heart failure	0.747	0.476–1.172	.2044	-	-	-
Peripheral vascular disease	1.143	0.615–2.122	.6723	-	-	-
Cerebrovascular disease	0.746	0.44–1.263	.2753	-	-	-
Chronic pulmonary disease	0.35	0.042–2.932	.3332	-	-	-
Diabetes mellitus	0.913	0.522–1.599	.751	-	-	-
Liver disease	0.434	0.145–1.296	.1345	-	-	-
Renal disease	0.665	0.307–1.443	.3019	-	-	-
Cancer	0.571	0.285–1.145	.1147	-	-	-
Others	0.761	0.322–1.747	.5197	-	-	-
Number of concurrent comorbidities	0.877	0.761–1.01	.0676	-	-	-
Active drug treatment						
Cardiac therapy	0.711	0.46–1.098	.1241	-	-	-
Antithrombotic drugs	0.886	0.603–1.301	.5364	-	-	-
Other antihypertensive drugs	1.249	0.483–3.233	.6461	-	-	-
β-blockers	1.239	0.795–1.929	.3438	-	-	-
Calcium channel blockers	0.806	0.498–1.304	.3787	-	-	-
Renin-angiotensin system antagonists	0.708	0.489–1.025	.0677	-	-	-
Cholesterol-lowering drugs	0.967	0.627–1.491	.8798	-	-	-
Selective β_2-adrenoreceptor agonists	0.35	0.042–2.932	.3332	-	-	-
Number of concurrent treatments	0.935	0.836–1046	.2412	-	-	-

Note: Odds ratios (OR) and 95% confidence interval (CI) for sustained ROSC in logistic regression models. Unadjusted univariate model and adjusted multivariate model with stepwise selection method. Data are available from 565 patients with known outcomes from the DENALI regional database.
Abbreviations: CCF, chest compression fraction; EMS, emergency medical services; Imp_{CC} variability, chest compression-generated thoracic impedance variability.
[a]Per 1 min increase in EMS arrival time.
[b]Per 100 U increase in Imp_{CC} variability, $mOhm^2$.

targeting a high CCF while minimizing chest compression pauses is strong, as interruptions in cerebral and coronary perfusions can alter survival and neurological prognosis as well as the probability of ROSC.[22,23]

Overall CPR quality delivered in our cohort showed a median CCF of 66%. In addition, a CCF ≥80% led to significant improvements in defibrillation success rate up to 60%, compared with lower CCF performances. Nonetheless, in our regression model, association between CCF and defibrillation outcome, ROSC or survival was not confirmed. This result can be a consequence of the small proportion of patients receiving CPR with a CCF < 60%, which might have made the impact of CCF on outcome less evident. Another explanation may be related to the intrinsic limitation of CCF itself that measures only the total CPR time spent in performing chest compression, without considering the efficiency of the compression delivered, in term of depth, rate, and recoil, which might have been of poor quality. CCF can arguably be considered as an isolated predictor of CPR outcome without a comprehensive evaluation of chest compression actions. This consideration potentially explains why the largest study on continuous compression versus 30:2 compression: ventilation, enrolling more than 23,000 OHCAs, was not able to show any difference in survival between the two interventions, despite a significantly higher CCF, 83% versus 77%, in the continuous compression group.[17] Thus, assessing Imp_{CC} variability may yield additional advantage in term of

TABLE 5 Logistic regression models for prediction of survival to hospital discharge.

	Unadjusted univariable model			Adjusted multivariable model		
Covariate	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Age	0.958	0.944–0.973	<.0001	0.957	0.942–0.972	<.0001
EMS arrival time[a]	0.924	0.857–0.997	.0405	-	-	-
Shock number	0.896	0.751–1.069	.2212	-	-	-
Gender (female vs. male)	0.620	0.366–1.048	.0743	-	-	-
Comorbidities						
Previous myocardial infarction	0.704	0.347–1.43	.3318	-	-	-
Congestive heart failure	0.690	0.390–1.218	.2006	-	-	-
Peripheral vascular disease	0.611	0.252–1.481	.2758	-	-	-
Cerebrovascular disease	0.516	0.248–1.072	.0763	-	-	-
Chronic pulmonary disease	0.757	0.09–6.363	.7979	-	-	-
Diabetes mellitus	0.595	0.274–1.291	.1886	-	-	-
Liver disease	0.199	0.026–1.493	.1163	-	-	-
Renal disease	0.383	0.115–1.273	.1173	-	-	-
Cancer	0.37	0.13–1.054	.0626	-	-	-
Others	0.311	0.073–1.329	.1151	-	-	-
Number of concurrent comorbidities	0.73	0.599–0.889	.0018	-	-	-
Active drug treatment						
Cardiac therapy	0.582	0.330–1.024	.0606	-	-	-
Antithrombotic drugs	0.757	0.469–1.222	.2545	-	-	-
Other antihypertensive drugs	0.85	0.243–2.977	.7993	-	-	-
β-blockers	0.953	0.548–1.658	.864	-	-	-
Calcium channel blockers	0.64	0.340–1.202	.1652	-	-	-
Renin-angiotensin system antagonists	0.824	0.526–1.291	.398	-	-	-
Lipid modifying agents	1.126	0.673–1.882	.6517	-	-	-
Selective β_2-adrenoreceptor agonists	0.757	0.09–6.363	.0023	-	-	-
Number of concurrent treatments	0.906	0,788– 1042	.1655	-	-	-
CCF, %	0.985	0.966–1.004	.1233	-	-	-
Imp_{CC} variability,[b] ms^2	1	0.997–1.003	.822	-	-	-

Note: Odds ratios (OR) and 95% confidence interval (CI) for sustained ROSC in logistic regression models. Unadjusted univariate model and adjusted multivariate model with stepwise selection method. Data are available from 565 patients with known outcomes from the DENALI regional database. Abbreviations: CCF, chest compression fraction; EMS, emergency medical services; Imp_{CC} variability, chest compression-generated thoracic impedance variability.

[a]Per 1 min increase in EMS arrival time.

[b]Per 100 U increase in Imp_{CC} variability, $mOhm^2$.

CPR quality since it targets all quality parameters of the chest compression maneuvers, with a specific pattern encompassing altogether different distinctive variables, such as compression rate, velocity, depth, release velocity, time, and pause length, in a single parameter. Having an Imp_{CC} variability on top of CCF during CPR might concurrently assure minimized pauses in compression with an overall goodness of the maneuver.

The theoretical benefit of an association between Imp_{CC} variability and clinical outcomes may be significant. Indeed, starting from the current observations, as Imp_{CC} variability is associated with defibrillation success, an optimization of this variable through a real-time CPR feedback may impact also long-term outcomes. In our perspective, the use of the Imp_{CC} variability should be intended not as a direct predictor of defibrillation success or outcome, but as a different indicator of the overall quality of chest compression maneuver.

4.1 | Limitations

This study has several limitations. First, this study had a retrospective design, enrolled only shockable OHCAs, and evaluated only the last part of the CPR effort. Accordingly, assessment of Imp_{CC} variability and its relationship with outcome remains to be proven prospectively and in different cohorts, including also nonshockable cardiac arrests.

Second, thoracic impedance waveforms recorded only by Physio Control AEDs were evaluated and no data on other chest compression parameters, that is, depth and recoil, were available. Third, additional factors accounting for large Imp_{CC} variations cannot be excluded, that is, pads movements, not proper skin-pad contact or different pads positions, length of CPR effort. Thus, this study has to be considered as proof of concept, while future prospective investigations, collecting also concurrent data on chest compression metrics, are needed to prove the role of Imp_{CC} variability evaluation during CPR, and also during training courses. Fourth, CCF was low in our cohort, that is, 66% in median, although above the recommended target of 60%.[4] However, this CCF was not representative for the whole CPR intervention, but only for the selected interval. Fifth, association of Imp_{CC} variability with long-term outcomes was not demonstrated in this study. One reason can stay in the population investigated that included only shockable cardiac arrests, known to have a better outcome; in addition, there were no data on bystander-initiated CPR, which represents another factor contributing to survival and functional recovery.[24] Impact of ventilation and different ventilation modes on Imp_{CC} is another aspect to be investigated. Finally, due to the lack of CPR metrics (i.e., depth, recoil) or physiological measurements (i.e., blood pressure, end-tidal CO_2, near infrared spectroscopy, etc.), outcomes (i.e., defibrillation success, survival) were used as the only read-out of the relationship between Imp_{CC} variability and quality of chest compression.[4] In addition, we are aware the Imp_{CC} variability calculated as total power might not be the best method to quantify the chest compression variability/consistency; indeed, other and more accurate algorithms might be developed starting from this proof-of-concept study. Nevertheless, the key message we want to highlight is that when assessing quality of chest compression, we should look not only at depth, chest recoil, pauses, and CCF only, but also at the overall consistency or harmony of chest compression maneuvers execution and for this purpose, the analysis of TTI waveform variability over time may represent a valid approach.

5 | CONCLUSION

This study revealed that Imp_{CC} variability can be used as a new CPR parameter to measure the consistency in chest compression execution. However, further studies are needed to confirm Imp_{CC} as a useful metrics for improving the quality of care and outcome in OHCA.

AUTHOR CONTRIBUTIONS

Conceptualization, G.R., A.M., F.F.; data analysis, V.C., G.M., G.Z., A.P., J.C., B.M.H.; data validation, A.M., C.F., B.M.H.; statistical analysis: C. F.; writing-original draft preparation, A.M., C.F.; writing-review and editing, F.F., G.S., G.R., M.M., G.M.S., A.C., G.G.; fundings, G.R., B.M. H.; supervision, G.R. All authors have read and agreed to the published ver-sion of the manuscript.

ACKNOWLEDGMENTS

The authors declare no conflict of interest.

FUNDING INFORMATION

The study was supported in part by the Horizon 2020 Program under grant agreement no. 733381 (EU Framework "European Sudden Cardiac Arrest network: toward Prevention, Education and New Treatment – ESCAPE-NET"). BMH has received funding from Region Skåne, Stig and Ragna Gorthon's Foundation, and Thelma Zoéga Foundation's fund for medical research.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Magliocca A, Castagna V, Fornari C, et al. Transthoracic impedance variability to assess quality of chest compression in out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand*. 2024;1-11. doi:10.1111/aas.14374