RESEARCH ARTICLE

Re-arrest immediately after return of spontaneous circulation: A retrospective observational study of in-hospital cardiac arrest

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Abstract

Background: Patients who achieve return of spontaneous circulation (ROSC) after in-hospital cardiac arrest (IHCA) may re-arrest. This phenomenon has not been sufficiently investigated. The aim of this study was to examine the immediate (1-min) and short-term (20-min) risks of re-arrest in IHCA.

Methods: We retrospectively analyzed four datasets of IHCA episodes, comprising defibrillator recordings collected between 2002 and 2022. Re-arrest was defined as the resumption of chest compressions following a period of ROSC after cardiac arrest of any duration. Parametric models were applied to calculate the immediate risk of re-arrest. In addition, we estimated the short-term risk of re-arrest within 20 min.

Results: In 763 episodes of IHCA, we observed 316 re-arrests: 68% to pulseless electrical activity (PEA), 25% to ventricular fibrillation/ventricular tachycardia (VF/VT), and 7% to asystole. Most re-arrests occurred with the same rhythm as in the initial arrest. When ROSC was achieved from a non-shockable rhythm, the risk of re-arrest to a non-shockable rhythm was initially 2% per minute and decreased to 1% per minute after 9 min. The corresponding risk of re-arrest to VF/VT was constant at 2% per minute. If ROSC was obtained from a shockable rhythm, the risk of re-arrest to a shockable rhythm was initially 5% per minute, decreasing to 4% per minute after

9 min. The corresponding risk to a non-shockable rhythm was constant at 1% per minute. The risk of re-arrest within 20 min was 27%, and the overall risk of at least one re-arrest per episode was 33%.

Conclusions: The immediate risk of re-arrest was approximately 2% per minute, with the highest risk occurring as a reversion to VF/VT if ROSC was obtained from VF/VT. The risk of re-arrest within 20 min of the initial arrest was 27%, and the overall risk of at least one re-arrest per episode was 33%.

KEYWORDS
cardiac arrest, IHCA, parametric models, re-arrest, ROSC

1 | INTRODUCTION

Return of spontaneous circulation (ROSC) is achieved in 40%–70% of patients with in-hospital cardiac arrest (IHCA), many of whom are critically ill and require intensive care.[1–8] These patients are at risk of re-arrest, defined as cardiac arrest (CA) after ROSC is obtained, including any non-perfusing state and rhythm.[9–11] International guidelines for advanced life support (ALS) provide a good framework for clinical decision-making.[12,13] Nevertheless, we lack knowledge about the risk of re-arrest in the minutes immediately after ROSC. Previous studies investigating the occurrence of re-arrest mainly focus on out-of-hospital cardiac arrest (OHCA), where it is reported that 18%–39% of patients obtaining ROSC will re-arrest.[10,14–18] Most studies on re-arrest after IHCA have used national registry data to investigate the occurrence of more than one CA event during a hospital stay, over a span of days and hours.[19,20] Bhardwaj et al. investigated the occurrence of re-arrest in a dataset combining episodes of OHCA and IHCA and reported that it was a common complication, occurring in 24% of CA patients after a median time of 5.4 h.[21]

Previous studies suggest that most patients who obtain ROSC after IHCA do so within the first 20 min.[3,4,22] The aim of this study was to examine the immediate (1-min) as well as the short-term (20-min) risks of re-arrest in IHCA, considering both the duration and the last observed state before ROSC.

2 | METHODS

2.1 | Study setting and population

We performed a post hoc analysis of four cohorts of adult patients (>18 years) suffering IHCA. The episodes were collected by emergency personnel at four different hospitals: St. Olav's University Hospital, Norway (two periods from 2009 to 2012 and 2018 to 2022), the University of Chicago Hospitals, USA (2002–2005), the Hospital of the University of Pennsylvania, USA (2008–2010), and the Penn Presbyterian Medical Center, USA (2008–2010). The episodes from Chicago and the first period at St. Olav's were analyzed as part of previous studies and later made available to us. All episodes from St. Olav's were collected for research purposes, while the episodes from the three US hospitals were collected as part of a quality assurance initiative.

The University of Chicago Hospitals (IL, USA) is an academic tertiary care facility. Two previously published studies investigated the quality of cardiopulmonary resuscitation (CPR) using a defibrillator with CPR-sensing capabilities.[23,24] The current study includes episodes of IHCA from these studies. In Chicago, episodes were excluded if the arrest occurred in the emergency department (ED) or the operating room (OR), as these areas were not covered by the resuscitation teams.[23] St. Olav's University Hospital (Trondheim, Norway) is an academic tertiary care facility. All adult IHCA occurring between 2008 and 2013 were collected as part of an earlier study investigating clinical state transitions.[3] We collected additional episodes between 2018 and 2022. The Hospital of the University of Pennsylvania and the Penn Presbyterian Medical Center are both academic medical centers. All IHCA at these two hospitals were collected between 2008 and 2010, with the only inclusion criterion being age >18 years. The researchers responsible for data collection at all sites contribute as co-authors.

2.2 | Data collection and handling

The data consist of defibrillator recordings, including a one-lead electrocardiogram (ECG) from the defibrillator pads, chest compressions, and ventilations during ongoing CPR. This information was combined with relevant details from patient records. The defibrillator recordings were manually assessed to determine the succession of clinical states during resuscitation. Details regarding the process of retrospective annotation of signal and event data from defibrillator files have been published earlier.[3,4,25] A recent methodological paper further elaborated on the potential utility of this approach.[26]

The start of an episode was defined as the time of the first registered chest compression, detected either as fluctuations in the transthoracic impedance signal or the compression depth signal.[27,28] We assessed the ECG during every compression pause to determine the clinical state of the patient.

ROSC was defined as a period of regular QRS complexes that lasted at least 1 min in the absence of chest compressions. It was

divided into two groups based on whether the rhythm preceding ROSC was shockable or not. As we do not possess measurements of invasive blood pressure, this 1-min cut-off is a pragmatic approach to retrospective ROSC detection, as the resuscitation team would hardly allow a hands-off time of that duration without the presence of a palpable pulse.

We defined re-arrest as the resumption of chest compressions subsequent to a period of ROSC. Sustained ROSC is defined in the Utstein guidelines as ROSC lasting more than 20 min.[3,4,29] Therefore, a new episode of IHCA was declared if the patient experienced a second CA after at least 20 min of ROSC.

PEA was defined as an ECG with regular QRS complexes with a frequency of ≥12 QRS/minute between compressions. This corresponds to at least one QRS every 5 s. Asystole was defined as an iso-electric ("flat") ECG line or as a rhythm slower than 12 QRS complexes per minute. This cut-off time was chosen to make it possible to distinguish PEA from asystole during a normal rhythm check. We categorized ventricular tachycardia (VT) and ventricular fibrillation (VF) based on their unique morphologies.[30] We knew from the patient record whether the patient obtained ROSC or was eventually declared dead at the end of an episode. Depending on this information, both ROSC and death were defined from the last compression recorded. The episodes from Chicago and the first period at St. Olav's (2008–2013) were annotated with the same exact criteria as part of a previous study.[3]

2.3 | Statistical methods and modeling

We investigated any potential time variability for the immediate risk of re-arrest by estimating the hazard of a spontaneous re-arrest (from ROSC) to either a shockable or a non-shockable rhythm that occurred within 20 min of the initial arrest. The hazard rate, or simply hazard, is defined as the conditional probability of a re-arrest in the next instant, given that the patient is still in ROSC. In the supplementary file, we show how the hazard approximately corresponds to the one-minute (i.e., immediate) probability for hazard values lower than 0.1. For example, a hazard of 0.02 corresponds to a one-minute probability of 2%. The shape of the hazard function for re-arrest over time could develop in several ways, for instance: rising, falling, constant, or unimodal (i.e., rising and then falling). A constant hazard can be modeled with the exponential distribution, while a monotonically rising or falling hazard can be modeled with the Weibull distribution.[31] The Greenwich and lognormal distributions are both suitable for modeling a unimodal course.[31,32] We compared these models for each type of re-arrest to find the most useful model while avoiding overfitting. This approach for model selection is described in detail in the supplemental material of a previous publication from our group.[25]

We used a Kaplan–Meier estimator to illustrate the proportion of patients remaining in ROSC up to 20 min.[33] A mixed-effects Poisson regression model with episode as a random factor was applied to estimate the total risk of re-arrest per episode, suitable for investigating events clustered within episodes.[34]

We applied the software Stata version 17 and R version 4.2.2 for all visualizations and statistical analysis.[35,36]

2.4 | Ethical aspects

This study is based purely on a retrospective analysis of observational data, and inclusion would neither benefit nor disadvantage the patient. All episodes were de-identified, and the patients remained anonymous during the subsequent data analysis.

The Regional Ethics Committee (REC) granted approval for the collection and analysis of data from both periods at St. Olav's University Hospital. The data collected at the Penn Presbyterian Medical Center and the Hospital of the University of Pennsylvania were provided to us in anonymized form, and the collection of these data was approved by the local institutional review board (IRB).

The present study also represents a novel analysis of anonymous data collected in Chicago between 2002 and 2005 and analyzed by Laerdal Medical in collaboration with the University of Stavanger, originally published in earlier studies.[3,24] The original Principal Investigators actively contributed as authors and obtained IRB approval for both primary and secondary analyses at their institutions. Additional ethical approval in Norway was not deemed necessary due to the purely observational and de-identified nature of the data, and the significant time that has elapsed since data collection.

3 | RESULTS

Defibrillator recordings from 763 episodes of IHCA in 703 different patients were included: 160 episodes from the first period at St. Olav's University Hospital (2009–2013), 203 from the second period at St. Olav's University Hospital (2018–2022), 159 from the University of Chicago Medicine, 187 from the Hospital of the University of Pennsylvania, and 54 from the Penn Presbyterian Medical Center. In the 763 episodes, 506 contained at least one period of ROSC.

An overview of the episode and patient characteristics is given in Table 1. The lower part of the table shows the absolute number of re-arrests stratified by the preceding state and the rhythm that patients presented with during the re-arrest. In the 316 re-arrests, 88% recurred to the last observed rhythm before ROSC if ROSC was obtained from a non-shockable rhythm, and 73% recurred to the last observed rhythm before ROSC if ROSC was obtained from a shockable rhythm.

Since both ROSC and re-arrests could occur multiple times during an episode, Figure 1 illustrates the distribution of episodes with ROSC (left) and re-arrests (right). We observed that 75% (n = 380) of the episodes with ROSC contained a single period, while 63% (n = 110) of the episodes with re-arrests included one such event.

The immediate, minute-by-minute, hazard of re-arrest may vary with time and possibly differ depending on the nature of re-arrest and the rhythm that preceded ROSC. Figure 2 shows the hazard functions for re-arrest to PEA or asystole depending on whether ROSC was

Patient characteristics (n = 703)			
Median age (years)	67 (IQR 56–77)		
Sex	401 male (57%)		
Episode characteristics (n = 763)			
Episodes containing at least one period of ROSC	506 (66%)		
Episodes containing at least one re-arrest	176 (23%)		
Monitored episodes	485 (64%)		
Obtained sustained ROSC	384 (50%)		
Presumed cardiac etiology	330 (43%)		
Survived to discharge	124 (16%)		
Rhythm of re-arrest			
PEA	216 (68%)		
VF/VT	78 (25%)		
Asystole	22 (7%)		
Re-arrests stratified by preceding state	To non-shockable	To shockable	Sum
ROSC from non-shockable	220	30	250
ROSC from shockable	18	48	66
Sum	238	78	316
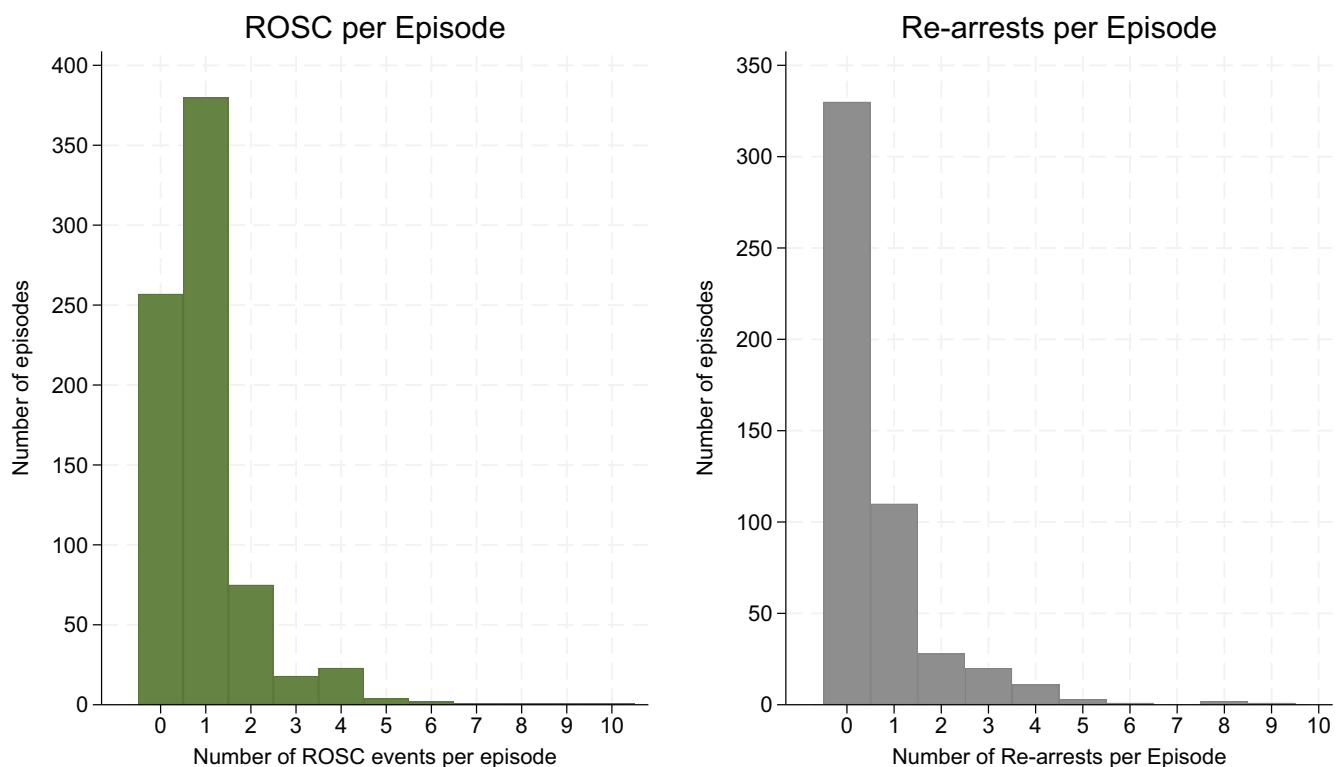
FIGURE 1 Distribution of the number of periods with return of spontaneous circulation (ROSC) and re-arrests per episode. Left: Histogram of the number of ROSC events across episodes. The majority of episodes had only one event. Right: Histogram of the number of re-arrests across episodes. Most episodes contained no or a single re-arrest.

preceded by a non-shockable (left graph) or shockable rhythm (right graph) during the first 20 min after the initial arrest. The hazard of re-arrest to a non-shockable rhythm, if ROSC had been preceded by a non-shockable rhythm, decreased slightly from 0.02 for the first 6 min to 0.01 from 9 to 18 min after the initial event of CA. If ROSC was preceded by VF/VT, the hazard of re-arrest to a non-shockable rhythm remained constant at 0.02.

Figure 3 shows the hazard of re-arrest to VF/VT depending on whether ROSC was preceded by a non-shockable (left graph) or a shockable rhythm (right graph). ROSC preceded by VF/VT had a
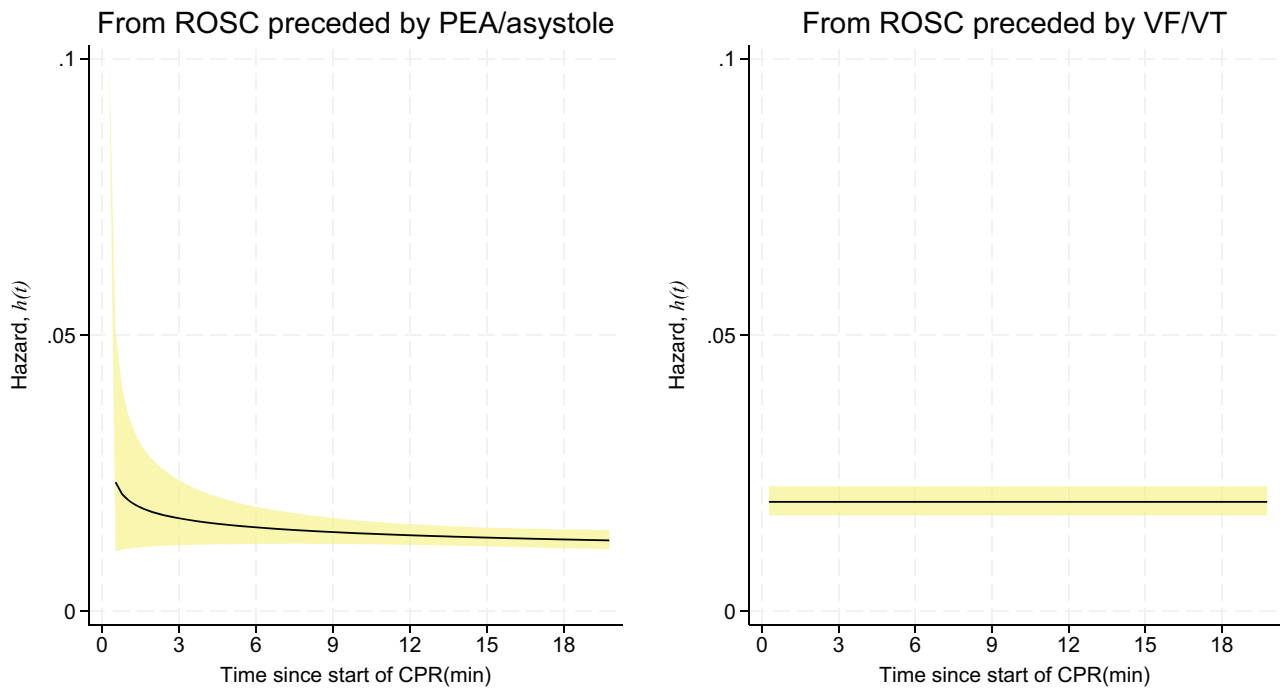
Re-arrest to PEA/asystole

FIGURE 2 Hazard functions with 95% confidence intervals (CI) for re-arrest to a non-shockable rhythm. Left: Hazard if return of spontaneous circulation (ROSC) was preceded by a non-shockable rhythm. Right: Hazard if ROSC was preceded by a shockable rhythm.
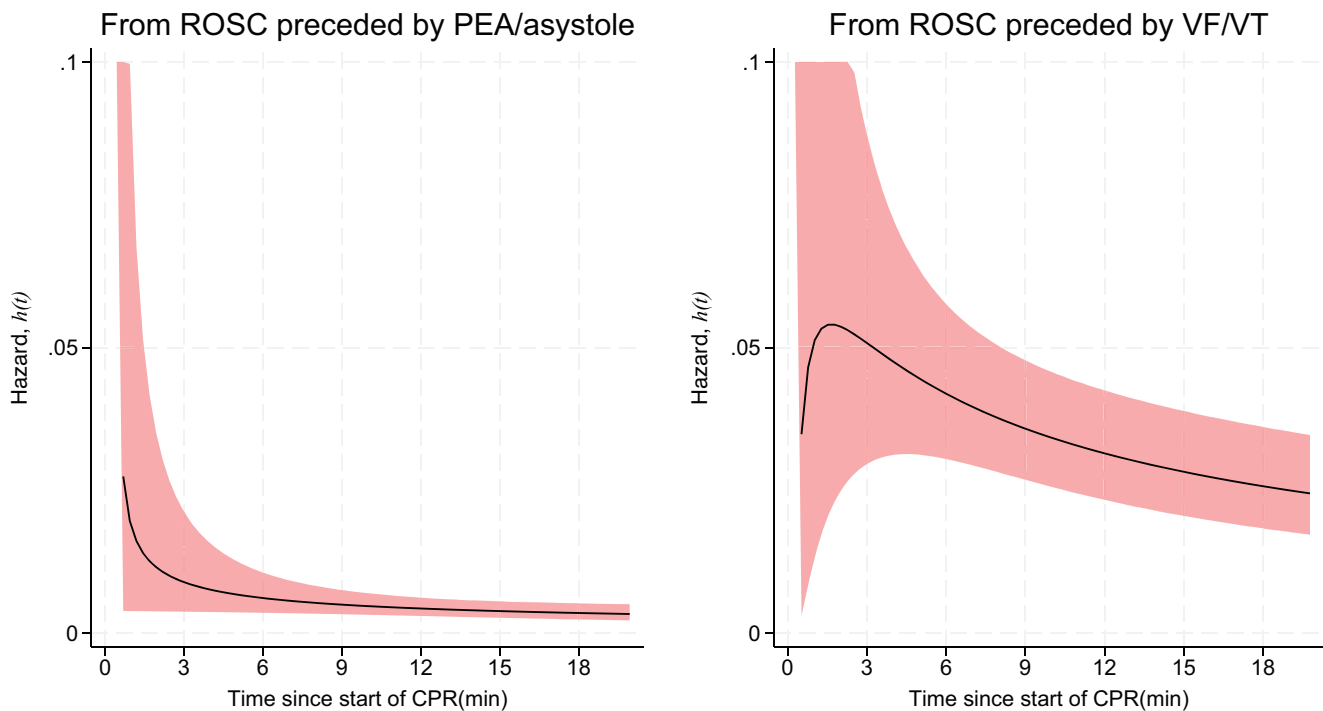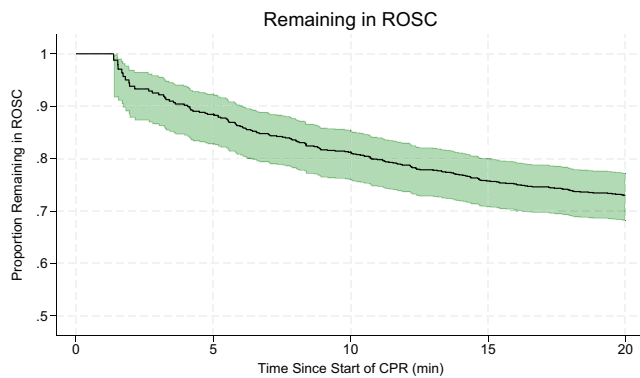
Re-arrest to VF/VT

FIGURE 3 Hazard functions with 95% confidence intervals (CI) for re-arrest to a shockable rhythm. Left: Hazard if return of spontaneous circulation (ROSC) was preceded by a non-shockable rhythm. Right: Hazard if ROSC was preceded by a shockable rhythm.

FIGURE 4 The proportion of patients who maintain return of spontaneous circulation (ROSC) over time after the initial arrest, amounting to 73% after 20 min. Only the first re-arrest per episode is considered. The green area represents the 95% confidence interval (CI).

hazard of 0.05 for re-arrest to VF/VT at 3 min, decreasing to 0.04 at 6 min and 0.03 at 12 min. The hazard of re-arrest to VF/VT, if ROSC was preceded by a non-shockable rhythm, decreased from about 0.02 during the first 6 min before stabilizing at 0.01 per minute.

At any one of the time points displayed in Figures 2 and 3, the hazard can be interpreted directly as the approximate probability of a re-arrest in the next minute. A patient who obtained ROSC from VF/VT and was still in ROSC 3 min after the initial arrest had an approximate 5% probability of a re-arrest back to VF/VT in the next minute (Figure 3). The same patient had a 2% probability of a re-arrest to a non-shockable rhythm (Figure 2). A patient who obtained ROSC from PEA or asystole and was still in ROSC 3 min after the initial arrest had a 1% probability of re-arrest to VF/VT (Figure 3) and a 2% probability of re-arrest to a non-shockable rhythm (Figure 2).

The total risk of re-arrest in the 506 episodes with ROSC can be reported in three distinct ways. Firstly, by the total number of observed re-arrests, which was 316 out of 506 episodes (62%; 95% confidence interval (CI), 58%–67%). Secondly, by the proportion of episodes that contained at least one re-arrest, observed in 176 of 506 episodes (35%; 95% CI, 31%–39%). Thirdly, by the mixed-effects Poisson model, which yielded an estimated expected proportion of 33% (95% CI, 26%–41%) with significant variability between episodes ($p < 0.001$).

Figure 4 provides an overall view of the process and illustrates the proportion of patients who were still in ROSC within 20 min of the initial arrest, amounting to 73% (95% CI: 68%–77%) after this period. This corresponds to a 27% probability of re-arrest within 20 min ($1-0.73 = 0.27$).

4 | DISCUSSION

This is the first investigation of the immediate and short-term risks of re-arrest from ROSC during IHCA. The main finding is that the immediate risk of re-arrest was approximately 2% per minute during the

first 20 min after the initial arrest, depending on the time since the initial event and the rhythm leading to ROSC. The probability of a re-arrest per episode was 27% within 20 min and 33% in total. As in OHCA, the rhythm of re-arrest primarily mirrored the initial rhythm.[10,18,37]

When considering the two analyses provided (immediate vs. total probability of re-arrest), it is important to note that they provide different kinds of information to the clinician at the bedside. The immediate, 1-min, perspective is highly dynamic, while the perspective of total probability within 20 min captures the episode as a whole. The latter thus disregards the different dynamics of shockable and non-shockable rhythms.

The highest risk of re-arrest was observed for re-arrest to VF/VT in patients who initially obtained ROSC from VF/VT, and the hazard decreased with time. The probability of re-arrest from ROSC preceded by PEA/asystole was lower than in the VF/VT group throughout the period of observation. In a clinical context, this reflects the fact that in-hospital VF/VT often receives early defibrillation, but that the underlying cause, for example, coronary ischemic events, is seldom treated at this point, and thus, they often re-arrest back to VF/VT. Bhardwaj et al. previously reported that 56% of patients who re-arrest after an initial arrest with VF/VT present with VF/VT again during their stay.[21] Furthermore, a shockable re-arrest rhythm is associated with a better outcome in OHCA.[10,16,38] In arrests with PEA, ROSC may be achieved when an underlying cause has been more or less reversed, and thus, the probability of immediate re-arrest may be lower.[4,39,40]

This study provides a description of reality and quantifies the risk of re-arrest after achieving ROSC. The findings correlate well with clinical experience and support the current practice regarding post-ROSC treatment.[41] Achieving ROSC from PEA indicates that the treatment of the underlying cause is on the right course. Nevertheless, if the patient re-arrests to PEA, a recent study from our group revealed that the probability of obtaining ROSC again in that scenario is quite high at 26% within the first 3 min.[25]

The observed short-term cumulative risk of re-arrest at 27% within 20 min is not trivial. Bhardwaj et al. reported that 24% of CA patients re-arrested during subsequent hospitalization when re-arrest was defined as the loss of pulse and receipt of CPR after ≥20 min of sustained ROSC.[21] Our finding of a similar re-arrest proportion within 20 min highlights the very dynamic nature of this early period. It is important to note that the total probability represents an average and is elevated by some patients who experience multiple events of ROSC and re-arrest. We get an impression of the magnitude of this phenomenon in Figure 1 and how this affects the results by comparing the total number of observed re-arrests (62%) with the proportion of episodes that contain at least one re-arrest (35%) and the estimate from the Poisson model (33%).

It is necessary to point out that PEA is a condition that cannot be diagnosed by ECG alone. ROSC and PEA may represent a continuum of increasing severity. Pulse palpation in either the femoral or carotid artery is the current method used to distinguish PEA from ROSC, although previous studies have shown that manual pulse palpation

can be inaccurate.[42-45] Measurement of end-tidal CO_2 ($ETCO_2$) is a helpful supplement, as an abrupt rise indicates ROSC.[46-49] A recent experimental study shows promising results from applying a non-invasive carotid Doppler to detect ROSC.[50] The European Resuscitation Council (ERC) recommends that intra-arterial blood pressure monitoring be established as a part of post-resuscitation care.[41] Investigating rates of re-arrest using the above-mentioned measurements would be an interesting topic for future studies.

5 | LIMITATIONS AND STRENGTHS

Due to the lack of objective circulation measurement, our retrospective classification of ROSC may have resulted in an underestimation, as we disregarded very brief periods of ROSC lasting less than 1 min. Furthermore, we included all data available to us, collected over 20 years at four different hospitals. This has two methodological consequences. Firstly, we lack information on all the circumstances of IHCA and do not possess data on missed IHCA cases. Secondly, the guidelines have been updated several times during the period, albeit mainly focusing on optimizing existing protocols and making defibrillators widely available.[13,51-53] Furthermore, we have estimated the risk of re-arrest at the population level rather than for individuals. The latter would require an approach similar to what Norvik and coworkers did when taking the ECG development during PEA into account.[54]

The primary strengths of this study include the unique availability of objective, time-stamped data from defibrillators, which closely reflect the real-time clinical conditions at the bedside. Additionally, the large sample size from four general hospitals ensures coverage of many different IHCA scenarios.

6 | CONCLUSION

The immediate risk of re-arrest from ROSC during IHCA was approximately 2% per minute. The short-term risk of re-arrest was 27% within 20 min and 33% in total. Patients tended to re-arrest with the same rhythm from which ROSC was initially obtained. The highest risk of re-arrest was to VF/VT if ROSC was obtained from VF/VT. Different risks of re-arrest may reflect the degree to which the underlying cause of CA has been addressed.

AUTHOR CONTRIBUTIONS

E. Unneland: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing—Original Draft, Visualization A. Norvik: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing—Review & Editing D. Bergum: Conceptualization, Investigation, Data Curation, Writing—Review & Editing, Supervision D.G. Buckler: Data Curation, Writing—Review & Editing A. Bhardwaj: Writing—Review & Editing T. Eftestøl: Writing—Review & Editing Elisabete Aramendi: Conceptualization, Software, Writing—Review & Editing T. Nordseth: Conceptualization, Investigation, Data Curation, Writing—Review & Editing B. Abella: Conceptualization, Writing—Review & Editing J.T Kvaløy: Methodology, Writing—Review & Editing E. Skogvoll: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing—Review & Editing, Supervision, Project administration, Funding acquisition.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

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