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REVIEW

Ethical challenges in resuscitation

Spyros D. Mentzelopoulos[1*], Anne-Marie Slowther[2], Zoe Fritz[3], Claudio Sandroni[4], Theodoros Xanthos[5,6], Clifton Callaway[7], Gavin D. Perkins[2], Craig Newgard[8], Eleni Ischaki[1], Robert Greif[9], Erwin Kompanje[10] and Leo Bossaert[11,12]

Abstract

Purpose: A rapidly evolving resuscitation science provides more effective treatments to an aging population with multiple comorbidites. Concurrently, emergency care has become patient-centered. This review aims to describe challenges associated with the application of key principles of bioethics in resuscitation and post-resuscitation care; propose actions to address these challenges; and highlight the need for evidence-based ethics and consensus on ethical principles interpretation.

Methods: Following agreement on the article's outline, subgroups of 2–3 authors provided narrative reviews of ethical issues concerning autonomy and honesty, beneficence/nonmaleficence and dignity, justice, specific practices/circumstances such as family presence during resuscitation, and emergency research. Proposals for addressing ethical challenges were also offered.

Results: Respect for patient autonomy can be realized through honest provision of information, shared decision-making, and advance directives/care planning. Essential prerequisites comprise public and specific healthcare professionals' education, appropriate regulatory provisions, and allocation of adequate resources. Regarding beneficence/nonmaleficence, resuscitation should benefit patients, while avoiding harm from futile interventions; pertinent practice should be based on neurological prognostication and patient/family-reported outcomes. Regarding dignity, aggressive life-sustaining treatments against patients preferences should be avoided. Contrary to the principle of justice, resuscitation quality may be affected by race/income status, age, ethnicity, comorbidity, and location (urban versus rural or country-specific/region-specific). Current evidence supports family presence during resuscitation. Regarding emergency research, autonomy should be respected without hindering scientific progress; furthermore, transparency of research conduct should be promoted and funding increased.

Conclusions: Major ethical challenges in resuscitation science need to be addressed through complex/resource-demanding interventions. Such actions require support by ongoing/future research.

Keywords: Resuscitation, Personal autonomy, Beneficence, Social justice

Introduction

Ongoing changes in medicine, and the societal context in which it is practised, create a range of ethical challenges for clinicians. Rapid progress in resuscitation science and intensive care provides increased opportunities to treat patients [1, 2], while an aging population and increased prevalence of people with multiple comorbidities raises questions about how much benefit these treatments can bring. Concurrently, there has been a move from paternalistic to patient-centered care with a more informed

*Correspondence: sdmentzelopoulos@yahoo.com; sdmentzelopoulos@gmail.com
[1] First Department of Intensive Care Medicine, National and Kapodistrian University of Athens Medical School, Evaggelismos General Hospital, 45-47 Ipsilandou Street, 10675 Athens, Greece
Full author information is available at the end of the article

The contributions of the second, third, fourth, and fifth author should be considered as equally important and equivalent to a contribution from a second author. The contributions of the sixth, seventh, eighth, ninth, tenth, and 11th author should be considered as equally important and equivalent to a contribution from a third author.

population and an increasing focus on individual rights and values. Key ethical documents and guidelines have both reflected and contributed to this change [2–6] and there is a substantial literature on the application of key ethical principles in resuscitation medicine [1, 3–15]; see also the electronic supplementary material (ESM)].

Evidence-based standards of emergency care and related ethical considerations should evolve simultaneously to ensure high-quality care [1, 5]. However, the interpretation of ethical principles in the context of resuscitation/end of life decision-making may vary among different countries and cultures for various reasons [1, 5, 16, 17].

The objectives of the current narrative review are to (1) describe current and emerging challenges associated with the application of ethical principles in resuscitation and subsequent critical care; a brief, pertinent summary is presented in Table 1, (2) propose possible ways, actions, and initiatives to address these challenges; and (3) highlight the need for research evidence-based ethics and international consensus [17] on the perception of ethical principles in relation to resuscitation.

We have defined the relevant ethical principles as follows:

- Autonomy: respect for the right of self-determination [1, 7].
- Honesty: accurate and transparent communication to the patient/family of the best research evidence, and clinical judgment including uncertainties.
- Beneficence: selection of beneficial interventions for the patient after assessment of the risk-to-benefit ratio [1, 3].
- Non-maleficence: avoiding harm or inflicting the least possible harm in the course of achieving a beneficial outcome [1].

Table 1 Common, major ethical challenges in resuscitation and associated principles of bioethics

Ethical dilemma/practice Issue[a]	Associated principle(s)
During cardiac arrest	
Should the patient receive CPR?[b]	Balance of beneficence/nonmaleficence vs. autonomy, dignity
When should I stop CPR?	Nonmaleficence; dignity
Is there legal support for AD/ACP?	Country-specific interpretation of autonomy
After ROSC	
Does patient clinical status/comorbidities justify LST?	Beneficence/nonmaleficence
How should I inform the family and involve them in decision-making?[c]	Honesty; autonomy; beneficence/nonmaleficence; dignity; justice
Is there legal and/or healthcare systemic support for AD/ACP?	Honesty; autonomy; Beneficence/nonmaleficence; dignity; justice
ICU care:	
When should I withdraw or withhold LST?	Nonmaleficence; autonomy, dignity
How should I involve the family and/or the patient in decision-making?[c]	Honesty; autonomy; beneficence/nonmaleficence; dignity; justice
Is there legal and/or healthcare systemic support for AD/ACP?	Honesty; autonomy; beneficence/nonmaleficence; dignity; justice
Healthcare system	
Do patients have equal access to the best quality of care?	Justice
Research	
Is autonomy of research participants respected?	Balance of autonomy vs. beneficence/nonmaleficence[d]
Is participants' risk exposure minimized?	Nonmaleficence
Is there a prospect of individual benefit for each participant?	Beneficence; justice
Is the burden of risk equally distributed among societal groups?	Justice
Are research subjects treated with the appropriate respect?	Dignity
Is the research conducted in a transparent manner?	Honesty; beneficence/nonmaleficence

Definitions for ethical principles are provided at the end of the introduction

The associations between clinical dilemmas/practice issues and ethical principles are analyzed throughout the text

CPR cardiopulmonary resuscitation; *DNACPR* Do not attempt CPR; *AD* Advance Directive; *ACP* advance care planning; *LST* life-sustaining treatment; *QoL* Quality of Life

[a] Challenges associated with other, specific, clinical practices/circumstances are presented in Table 4

[b] Patient consent for CPR is presumed, unless there is immediate access to or prior knowledge of recorded patient wishes against CPR (see also text and Table 2); as further analyzed in the corresponding article subsections, recorded patient preferences are normally associated with an AD or ACP

[c] This should include a shared decision-making process as further analyzed in the text

[d] Clinical research may evaluate new and potentially beneficial interventions, or even routine practices (e.g., epinephrine use during CPR) with a still unclear risk-to-benefit relationship

- Dignity: comprises "*being human*", "*having control*", "*relationship and belonging*", *and* "*maintaining the individual self*" [1, 18]; regarding resuscitation and postresuscitation care, dignity means avoiding disproportional interventions and an "end-of-life" contradicting patient's preferences.
- Justice: means fair and equal distribution of benefits, risks, and costs; pertains to the equality of rights to healthcare, and the legal obligation of healthcare providers to adhere to appropriate care and allocation of burdens and benefits [1].

Repecting patient preferences

Means to safeguard the autonomy of incapacitated cardiac arrest patients include advance directives, advance care planning (ACP), and consulting their trusted/loved ones to establish previously expressed wishes. Advance directives and ACP frequently concern an individual's preferences regarding cardiopulmonary resuscitation (CPR) and other life-sustaining treatments (LSTs) [19].

Advance directives

Advance directives address cases of patients with loss of decisional capacity and include living wills (instruction directives) and appointment of a "health care proxy" with durable power of attorney to make healthcare decisions (proxy directive) [1, 10, 19, 20]. Instruction directives may comprise summary/general or detailed/specific descriptions of the patient's values, goals, and preferences regarding healthcare issues and interventions [1, 11, 19, 20]. Specific preferences may include do-not-attempt CPR (DNACPR).

Healthy individuals drafting living wills may attempt to cover a broad spectrum of diseases, without having the required "medical knowledge and a grasp of the resulting conditions" [21]. This may result in ambiguity of the directive, challenging its applicability, and necessitating interpretation under specific clinical conditions [20]. Advance directives' legal status depends on cultural, religious, sociolinguistic, political, and medico-ethical factors [22], and varies widely among European countries from "*not mentioned in law*" to "*legally binding*" [6, 20].

Living wills drafted during health may not reflect changing preferences due to aging, occurrence of serious illness, and/or cognitive decline [23–25]; such factors may also affect the physicians' preferences about their own healthcare [25]. However, >70% of elderly inpatients with previously stated resuscitation preferences may ultimately wish their family and physician decide for them [26]. Conversely, recent evidence suggests that advance directives may promote comfort care and prevent end-of-life overtreatment [27]; this is consistent with nonmaleficence and dignity.

ACP

Advance directives and ACP exhibit major differences. ACP focuses on shared decision-making between clinician and patient. It is a dynamic, iterative process of eliciting and recording informed preferences of patients about end-of-life care, and accordingly pre-specifying and prioritizing future treatment goals. This is achieved through communication among patients, trained healthcare professionals, family, and other loved ones [28]. ACP may help the patient cope with death, and alleviate ethical burden from and strengthen relationships with his/her loved ones [29].

Recent evidence on complex and resource-demanding interventions (see ESM) suggests that ACP promotes congruency of care with patients wishes and associated patient and/or family satisfaction; reduces family stress, anxiety and depression; and may reduce the overall rates of "aggressive" LSTs [28], which accords with nonmaleficence and dignity. The effective linking of patients' wishes to realizable care plans requires multifaceted approaches (e.g., the Physicians orders for LSTs (POLST) forms/registry [30]) and a specific healthcare policy of enacting supportive regulations and making recorded patients' preferences and goals easily accessible to emergency caregivers [31].

Integration of DNACPR preferences with ACP—which includes patient preferences about outcomes and/or other treatments (besides resuscitation)—has been advocated to help address major issues currently associated with "isolated" DNACPR orders [8]. Such problems include lack of participation of patient/family in decision-making [8], inappropriate CPR [3, 4, 6, 8] or CPR resulting in poor, patient-perceived quality of life [1], and withholding of other indicated treatments such as pain relief and fluid intake [8]. Withholding of indicated treatments is related to misinterpretation of DNACPR and is not ethically justified [32].

Consent for interventions and shared decision-making

Article 5 of the Biomedicine Convention states that "*An intervention in the health field may ONLY be carried out AFTER the person concerned has given free and informed consent to it*" [33]. Consent validity may depend on (1) an individual's ability to understand essential information about their illness and indicated treatment, appraise the gravity of their condition, compare risks and benefits, and express a rational choice [10]; (2) availability of adequate time to decide [14]; and (3) concurrent emotional stress [15]. In emergency situations such as cardiac arrest, and in the absence of any readily accessible, CPR-specific, recorded patient preferences and/or DNACPR orders, immediate necessity dictates a "treat first, discuss later" approach (Tables 1, 2).

Table 2 Characteristics of OHCA and IHCA potentially influencing Autonomy and Beneficence/Nonmaleficence

	OHCA	IHCA
Onset and etiology	Sudden and most often of presumed cardiac etiology (E56 and E57 of ESM); victims often not likely to have considered drafting advance directives and/or advance care planning	Often preceded by initiation of invasive monitoring and LSTs (e.g., vasopressor support or mechanical ventilation), aimed at managing life-threatening, conditions, such as respiratory or circulatory failure of frequently noncardiac etiology (E58 and E59 of ESM); Victims may be more likely to have considered drafting advance directives and/or advance care planning, especially in the presence of multiple comorbid conditions potentially aggravating prognosis (8; E47 and E48 of ESM)
Clinical status and comorbidities	Often unknown when CPR is started	Generally known and reported in the clinical chart
Advance directives	Most often unknown to rescuers; Resuscitation normally proceeds under presumed, patient consent	LST Directives normally known to attending physician, and accessible by the hospital's resuscitation team
ACP	Most often unknown to rescuers; Resuscitation normally proceeds under presumed, patient consent; in certain healthcare systems, forms containing patient preferences may be accessible by the EMS rescuers (9, 26; E33 of ESM)	Patient preferences regarding LST normally known to attending physician, and accessible by the hospital's resuscitation team
DNACPR orders	Most often unknown whether there would be a DNACPR order in place if the patient had experienced an IHCA; Patient comorbidities and general health status/QoL are also unknown, unless a pertinently informed person such as a family member is present on the scene; Resuscitation normally proceeds under presumed patient consent	Normally recorded and accessible by the hospital's resuscitation team
CPR providers	Doctors and nurses but also paramedics or firemen, according to the EMS organisation	Doctors and nurses
Prediction tools potentially useful for decision making	Termination of resuscitation rules before transport to hospital	Clinical scores to predict the chances of neurologically intact survival before CPR or after ROSC

IHCA in-hospital cardiac arrest; *OHCA* out-of-hospital cardiac arrest; *CPR* cardiopulmonary resuscitation; *ACP* advance care planning; *ESM* electronic supplementary material (with additional references); *LST* life-sustaining treatments; *EMS* emergency medical services; *DNACPR* do not attempt cardiopulmonary resuscitation; *QoL* quality of life; *ROSC* return of spontaneous circulation

In challenging cases of ongoing, postresuscitation patient incapacity and absence of any associated, advance directives or ACP, decisions on LSTs should reflect the result of a collaborative process enabling shared-decision making of surrogates and clinicians after considering the available evidence [34] and the patients' values goals and preferences [9, 10]. Other challenges may include accuracy of surrogates' estimates of patient preferences [35], potential subjectivity of physicians predictions for post-discharge, health-related quality of life (QoL) [36], and possible disagreements/conflicts between surrogates of equivalent standing and/or between surrogates and clinicians [37]; in the absence of recorded, informed DNACPR preferences, physician-issued DNACPR orders based on poor prognosis may occasionally contradict surrogates' overoptimistic expectations from aggressive LSTs [1, 6]. Conflicts—if not timely resolved (e.g., with the aid of an Ethics Committee)—may lead to indecisiveness regarding indicated treatment(s) and poor patient outcomes [37].

Presenting information for decision making

An essential prerequisite for autonomy is the informed and meaningful patient/family involvement in decision-making. In the context of honesty, the physician should:

(a) Present all options and likely outcomes in a clear and comprehensible manner [7]. Failure to thoroughly discuss with surrogates comfort care alternatives to aggressive care may lead to therapeutic decisions that do not accord with patient preferences [38].
(b) Discuss the relation between resuscitation intervention-associated burden and benefit, preferably by using individualized choice architecture; this includes a hierarchical presentation of treatment options starting from the most appropriate according to physician judgment [39].
(c) Actively engage in religious/spiritual discussions as pertinent end-of-life concerns may substantially affect surrogates' decisions; a multicenter, prospective, cohort study suggested that intensive care professionals frequently fail to address such concerns [40].
(d) Ensure that the patient/family is given sufficient time to consider options, weigh up risks and benefits, and consult with others [41].

Models for predicting survival from attempted CPR have been developed and internally validated using large, in-hospital registry data sets [34]. However, the communication of statistical estimates of risk for poor outcome to patients/families may prove challenging, depending on their ability to comprehend the message, their beliefs about their individual risk relative to the general population, and the elicitation of emotional reaction(s) [42]. Furthermore, even if probabilistic outcomes could be accurately conveyed, the reality of a prolonged recovery period in a neurologically deficient state may be difficult to predict [43]. Uncertainties about the potential severity and duration of disability should be disclosed.

Physicians may feel torn between the desire to present a "full picture"—including that of limited resources—in order to meet stringent criteria for respecting patient autonomy, and the desire to protect patients from anxiety and burdensome decision-making while they are already unwell; occasionally, doctors may exercise a "therapeutic privilege" and withhold some information [44] about a resuscitation decision.

Benefiting without harming

Since medical interventions are potentially harmful, physicians should ensure that the balance favors benefit. The ethical challenge arises because of uncertainty about potential benefit and harm that might occur in an individual case. This is increased in situations where patients cannot communicate and their views on potential benefits and harms of interventions are unknown. In the context of CPR, these ethically difficult decisions occur when considering initiating CPR, terminating CPR and limiting LSTs following return of spontaneous circulation (ROSC).

There is a potential risk of harm during/after CPR. Data from 27 European countries suggest that among patients resuscitated from out-of-hospital cardiac arrest (OHCA), 75% (individual, country-reported range, 50–90%) do not achieve ROSC before hospital admission; and the overall, in-hospital/30-day mortality rate amounts to 90% (country-reported range, 69–99%) [45]. Similar mortality data have been reported for the United States and Canada (year 2010, in-hospital mortality, 90%; region-specific range, 81–94%) [46] and Australia (year 2015, in-hospital/30-day mortality, 88%; region-specific range, 83–91%) [47]. In OHCA survivors to hospital discharge, hypoxic-ischemic brain injury (HIBI) frequently results in long-term cerebral disability, including persistent vegetative state [48]. Among Australian patients aged ≥ 65 years, the estimated proportion of moderate-to-severe neurological disability or death at 12 months postarrest amounted to 44% [49]. Predicting when CPR is unlikely to result in a neurologically meaningful survival and knowing in advance the patient values and preferences is crucial to prevent harmful resuscitation efforts. This is difficult to achieve, especially in OHCA which is more unpredictable, with little available information about the patient's clinical status or personal wishes. The default is therefore to start CPR immediately in all

OHCAs, unless obvious signs of irreversible death are present or when there is a valid advance directive or a DNACPR order (Tables 2, 3, 4, 5). The ethical default is to preserve life and defer assessments of best interests until relevant information is available.

Conversely, for in-hospital cardiac arrest (IHCA), most events are witnessed and/or monitored and life support from healthcare personnel is immediately available. DNACPR may be in place in those in whom attempted CPR would probably be unsuccessful (Table 2; see ESM) In a recent survey, DNACPR orders were used in 22/32 European countries (69%) [5]. IHCA differs from OHCA in terms of patients' prearrest, acute/chronic comorbidities, prearrest therapeutic interventions, cardiac arrest-precipitating cause, and prognosis (Table 2). In the United States, the 2009 risk-adjusted, in-hospital mortality was 78%; among survivors, the proportions of clinically significant and severe disability were 28 and 10%, respectively [50]; risk-adjusted, in-hospital mortality varies widely among hospitals, i.e., from 68% to 100% [51].

If initial resuscitative efforts are unsuccessful the original assessment of pertinent benefits and harms should be reviewed. The European Resuscitation Council's (ERC's) ethical guidelines suggest that healthcare professionals should consider terminating resuscitation efforts in cases of asystole for >20 min despite ongoing advanced life support, in the absence of a reversible cause [3]. In general, survival with good neurological outcome is unlikely when OHCA duration exceeds 30 min [3]. However, this rule is not universal (see ESM) and it has been recently challenged by the advent of extracorporeal CPR [52]. Regarding IHCA, clinical decision aids have been proposed (34; see above and ESM); however, a large-scale external validation of the associated clinical scoring system is still pending.

Assessment of HIBI severity can guide the ethically difficult decision of whether and when to avoid disproportionate care for these patients. In 2014, guidelines for neurological prognostication after cardiac arrest were co-issued by the ERC and the European Society of Intensive Care Medicine [53]. These guidelines are based on a multimodal approach combining clinical examination and relevant investigations to predict poor neurological outcome with the greatest possible accuracy in patients who are comatose with absent or extensor motor response to pain at ≥3 days after ROSC. However, the quality of evidence supporting these predictors is low or very low and when prognosis appears to be indeterminate, or indicators give contradictory results, prolonged LST may be indicated.

Another limitation of neurological prognostication indices is the inconsistency in definitions of what represents a poor neurological outcome [54]: the QoL reported by cardiac arrest survivors or their caregivers is generally lower than that described by traditional outcome measures [55]. When assessing the appropriateness of resuscitative interventions, prognostication aids should be based on patient-reported and/or family-reported rather than clinician-reported outcomes. Cardiac arrest studies should include QoL measures and assess patient/family-reported outcomes [56, 57].

Optimizing end-of-life treatment

Successful implementation of ACP with support by the next-of-kin and attending physicians should result in efficacious, end-of-life comfort care.

In postresuscitation care, LST is often withdrawn based on shared decision-making [9, 10], and/or when the likelihood of neurologically favourable survival is extremely low [34], and clinical evidence indicates "disproportionate use" [58]. The distinction between allowing a patient to die after LST withdrawal and deliberate termination of life remains unanswered. Many doctors believe that a ventilator-dependent patient is allowed to die after LST withdrawal due to the underlying patient's condition or severe organ failure. Others regard LST withdrawal as the immediate cause of death as most patients die within the next 30 min [59]. Varying viewpoints on LST withdrawal may reflect cultural/religious influences [22]. Distressing symptoms should be anticipated and alleviated by sedatives and opioids; these agents do not seem to shorten the dying process [60]. Current European guidelines are consistent with palliative sedo-analgesia to reduce patient awareness of pain and suffering, without hastening death [10].

Equal access to best-quality care

Cardiac arrest patients should be provided with the same, timely, and high-quality resuscitation and postresuscitation care. Contrasting this ideal, a tenfold, intercontinental variation in reported OHCA incidence and outcomes (e.g., overall survival to hospital discharge from approximately 1% to 10%) has been previously documented [61].

As detailed above, OHCA outcomes vary greatly among European countries; this may be attributable to between-country differences in emergency care organization and quality, and availability and allocation of resources [1, 5, 45]. In North America, substantial, regional differences in OHCA in-hospital mortality may be partly explained by variable bystander CPR rates, and differences in the quality of postresuscitation care among hospitals ([46, 62]; see ESM).

In Europe, emergency care quality seems to be affected by patient comorbidity and age, and location (e.g., urban or rural) and type (e.g., teaching, tertiary care) of admitting and/or treating hospital ([5]; Table 3). Urban versus

Table 3 Issues of justice related to cardiac arrest, separated by OHCA versus IHCA

	OHCA	IHCA
Location	Public versus private location	In-hospital location at time of cardiac arrest (e.g., emergency department, ICU, ward, clinic)
	Rural versus urban; Type of admitting/treating hospital (academic/university, private/community, public)	Type of treating hospital (academic/university, private/community, public)
	Country, city, and county	
System	Organization, physician oversight, efficiency, staffing models, paid versus volunteer providers, quality assurance programs.	Organized response (e.g., rapid response teams) versus haphazard hospital coverage (single physician covering entire hospital for arrests), staffing, continuous quality improvement efforts
	Different staffing models at night and on weekends	
	Tracking of outcomes with timely feedback providers	
	Community focus on bystander CPR, availability and use of AEDs	Hospital focus on early provider recognition of pre-arrest state and standardized activation plan
	Availability and use of standardized forms for patient end-of-life wishes (e.g., POLST form) to guide resuscitation and interventions	
Provider	EMS provider level of training and education	Presence of standardized provider resuscitation training
	Paid versus volunteer	Financial incentive/stipend for covering hospital arrests
	Provider bias (e.g., age, race, religion, ethnicity, citizenship status); provider judgment based on patient factors (e.g., age, comorbidity burden) regarding likelihood of success with resuscitation influencing quality of resuscitation	

IHCA in-hospital cardiac arrest; *OHCA* out-of-hospital cardiac arrest; *ICU* intensive care unit; *CPR* cardiopulmonary resuscitation; *AED* automated external defibrillator; *POLST* physicians orders for life-sustaining treatments; *EMS* emergency medical services

Table 4 Ethical Challenges pertaining to Specific Clinical Practices or Circumstances

Specific practice or condition[a]	Ethical dilemma/practice issue[a]	Applicable principles	Relevant ESM references
FPDR[b]	Psychological trauma to family members[b]	Family autonomy	E77–E90
	Distraction/performance anxiety of resuscitation team[b]		
	Physical/psychological or medicolegal consequences for emergency caregivers[b]		
Pediatric/neonatal resuscitation	Child's/neonate's best interest might conflict with parent's/guardian's rights	Beneficence vs. nonmaleficence;	E90–E95
	Autonomy by proxy may result in futile CPR prolonging the patient's suffering	Autonomy	
	Prognostication may be difficult in preterm neonates		
Slow code	"Symbolic" resuscitation is unethical, despite arguments that it helps families to deal with the loss of their loved one	Nonmaleficence; honesty	E96, E97
Ensuring provider safety	Should take priority over any resuscitative procedure	Justice	E90, E98
Organ donation	This practice can result in aggressive resuscitation for the survival of the donor's organs	Nonmaleficence	E99
"Very recent" (i.e., ≤ 2 years) immigrants/refugees	Such patients may be more likely to receive end-of-life aggressive care compared to long-standing residents	Nonmaleficence; justice; dignity; autonomy	E100

ESM electronic supplementary material, *FPDR* family presence during resuscitation; *CPR* cardiopulmonary resuscitation

[a] A more detailed presentation is provided in the ESM

[b] Recent evidence (ESM's references E83–E85) supports FPDR in the presence of caregivers skilled in providing family support; FPDR policies could be developed within the broader context of family-centered care (ESM's reference E87)

rural location (e.g., in Japan; see ESM) can impact the available workforce, quality and frequency of provider training, volume of emergency care resources, and response time (due to geographic dispersion, distance, and ambulance availability). In the United States, the combination of low income and black race seems to negatively impact bystander CPR rates [63]; these findings cannot be generalized to other racial or ethnic groups, given the scarcity of relevant studies. Collectively, these challenges represent inequalities in access, treatment, and outcome.

Access to specific hospital resources (e.g., targeted temperature management, post-ROSC cardiac catheterization, extracorporeal CPR) are labor-intensive, expensive, and require specialized personnel with wide variation in availability. Even among high-resource countries with wide implementation of extracorporeal CPR, this resource is expectedly concentrated in urban tertiary hospitals with availability of advanced cardiovascular care (see ESM). Out-of-hospital use of extracorporeal CPR is even less common and generally restricted to Emergency Medical Services systems staffed by physicians with mobile intensive care unit capability [64].

Focusing on improvement and consistent provider training, bystander CPR, availability and use of automated external defibrillators, and more standardized resuscitation practices would improve the justice of resuscitation. Modifying system-level factors likely require a central champion, dedicated funding, and organizations that are receptive and malleable to change. There is evidence that improvement in survival from cardiac arrest can improve over time with heightened focus on system factors, feedback, quality of CPR, tracking outcomes, and training [46].

Rationing in resuscitation presents challenges regarding the objectivity and ethical integrity of criteria applied for DNACPR/LST decisions [65]. Utilitarian allocation of limited resources can be based on futility and/or differences in prognosis/LST cost [65, 66]. Futility has been defined as "*the use of considerable resources without a reasonable hope that the patient would recover to a state of relative independence or be interactive with their environment*" [65]. However, without quantification of "*considerable*", "*reasonable*", "*relative independence*", and "*interactive*", beneficial treatment can be arbitrarily/unethically denied to vulnerable population subgroups such as the elderly, the disabled, or those with chronic or hereditary or genetic diseases/anomalies [65].

Table 3 displays OHCA versus IHCA differences concerning justice.

Specific clinical practices or circumstances

These include family presence during resuscitation, pediatric/neonatal resuscitation, slow code, provider safety, organ donation, and end-of-life treatments for "very recent" (i.e., ≤ 2 years) immigrants/refugees. Ethical challenges are summarized in Table 4 and detailed in the ESM.

Ethical issues in emergency research

In cardiac arrest research, respect for autonomy is challenging, because the immediate necessity for resuscitation precludes obtaining pre-enrollment, informed consent [13, 14]. For low-risk research [13], ethically/publicly acceptable, alternative consent models include deferred consent, and exception to informed consent (EFIC) with prior community consultation [13, 67]. In deferred consent, the patient or his/her next-of-kin or legally authorized representative are informed about the study as soon as possible and informed consent for continued participation is requested; this consent model can be applied in emergency research involving incapacitated patients in the European Union [13]. If the patient dies before the next-of-kin can be reached, practices may vary based on weighing transparency and informing the relatives against the associated burden/harm. In EFIC, information is shared with the relevant communities and community members are provided with the opportunity to opt out by requesting "No Study" [68]; this consent model can be used in emergency research in the United States [13; ESM]. Table 5 displays the characteristics of these consent models and associated ethical challenges, including the issue of consent validity [1, 13–15]. Additional consent models such as integrated consent and prospective consent have been detailed elsewhere [1]. Once enrolled in a trial, withdrawal of consent may introduce bias, as those doing less well are more likely to withdraw [69]. Some authorities (e.g., United States Food and Drug Administration) but not all (e.g., European Union authorities) forbid participants from withdrawing data that have already been collected up to the time that they rescind their consent. Additional challenges are detailed in the ESM.

Commercial and noncommercial academic research

Efforts to address issues of flawed study design, selective reporting, "ghostwriting", and "guest" or "gift" authorship (see ESM) have included compulsory, pre-enrollment registration of trial protocols, posting of results to trial registries, and journal publication within 12 and 24 months of trial completion (respectively), and a call for disclosure of results from still-unreported trials [70]. Furthermore, journals oblige authors to detail the sponsor's role and their own contributions as regards study conception, design, and conduct, data analysis and interpretation, and manuscript preparation and approval for submission.

Another major issue concerns prioritization of research according to public health need. Despite recently confirmed steady improvements, cardiac arrest outcomes still remain dismal [45–47, 49–51, 71]. Considering the pertinent public health mortality burden, cardiac arrest resuscitation guidelines are based on 35–53 times lesser randomized clinical trials per 10,000 deaths per year as compared with guidelines for myocardial infarction, heart failure, and stroke [71]. Research on high-cost, patent protected drugs or devices has received disproportionately higher industry and/or governmental funding relative to much-needed, non-commercial, academic resuscitation research on patent-unprotected, low-cost, widely used drugs of still-uncertain efficacy, such as epinephrine, or antiarrhythmics [71].

Addressing major challenges—future directions

At global level, the respect for patient values, preferences, and goals varies according to country-specific, or region-specific balance between paternalism and patient-centricity. Cultural, religious, legal, and socioeconomic barriers would have to be overcome to apply harmonized policies supporting resource-demanding approaches (e.g., POLST [31, 32]) so as to effectively safeguard patient autonomy.

Examples from regions such as Oregon, United States [31, 32] suggest that provision of information to the public in an "unbiased manner", preferably through organized and "*free-of-charge*" education on the benefits and limitations of resuscitation as well as knowledge of illness prognosis at individual level, may help patients (and their families) articulate their wishes. Patients and their loved ones should also be clearly aware of their rights emanating from the key ethical principles, as well as of the extent of these rights. Such actions and initiatives could benefit the society in general, and vulnerable groups (e.g., persons with poor socioeconomic status, and new immigrants/refugees) in particular.

Currently active caregivers should receive ethical practice training followed by predefined, skill-level certification so as to integrate the respect for autonomy and the other ethical principles in their daily practice. This would likely promote convergence to a more uniform interpretation of key principles amongst physicians and nurses and facilitate the application of currently recommended, structured, shared decision-making procedures [9, 10] in a preferably standardized manner. In addition, teaching of Medical Ethics at the pre-graduate level would equip the forthcoming generations of physicians and healthcare professionals with adequate theoretical knowledge

Table 5 Characteristics of consent models used as alternatives to pre-enrollment informed consent (IC) Adapted with permission from reference [1]. ESM, electronic supplementary material (with additional references)

IC model	Prerequisites	Advantages	Associated challenges
Deferred IC (E08 of ESM)	Life-threatening condition—inability to obtain patient IC	It respects the patients' autonomy, and enables the conduct of much needed emergency research [13]	Absence of legal definition of consent for procedures that have occurred previously [13, 14]
	Potential for direct, research-related benefit to the patient or alleviation of suffering, or improvement in the diagnosis of his/her condition		
	Inability to obtain a valid, pre-enrollment IC from the patient's LR	Not excessively resource demanding	Potential discrepancies between patients and their surrogates regarding willingness to grant IC (E8 of ESM)
	Investigator not aware of any previously expressed patient objections with respect to clinical trial participation		
	The LR must be informed about the study as soon as possible[a]	It ensures "balanced" application of the principles of bioethics [13]	Surrogate IC validity may be affected by their ability to comprehend the study protocol under conditions of psychological stress, and uncertainty about the patient's outcome [10, 15]; previously recommended time frames for the surrogates IC decision were within 4–24 h [14]
	The clinical trial relates directly to the patient's medical condition		
	The clinical trial may be conducted exclusively in emergency situations		
	The clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject's condition		
EFIC with Community Consultation (E109 of ESM)	Life-threatening condition	Fast recruitment of a great number of patients. (E5 of ESM)	Respect for autonomy applied at community-level but not at patient-level
	Current treatments are unsatisfactory or unproven	Opt-out options may be feasible [68]	Public disclosure and community consultation has been associated with very low (i.e. 5%) levels of trial awareness among actual participants (E111 of ESM)
	Need for new and valid evidence for treatments		
	Inability to obtain pre-enrollment IC		
	The patient's LR must be informed about the study as soon as possible		
	Possibility of direct subject benefit from research participation		
	Inability to conduct the research without the waiver		
	Definition of therapeutic window for contacting an LR		
	Research ethics		
	Committee approval of IC procedures		
	Public disclosure and community consultation		

EFIC exception to informed consent; *LR* legal representative

[a] Practices may vary in cases of patient's death occurring before the LR can be reached (see also text)

(including *clear definitions*) of the key principles and of how they should be applied; this should be followed by ethical practice training and pertinent certification.

Ethical practices terminology should be harmonized to improve communication among involved parties and prevent confusion. For instance, consensus should be reached about the most suitable of acronyms denoting withholding of resuscitative interventions such as DNACPR, or DNAR (do-not-attempt resuscitation), or DNR (do-not resuscitate). In addition, potential conceptual differences between withholding and withdrawing of LST should ideally be clearly defined based on the broadest possible consensus. Some ethicists regard LST withdrawal as active causation of death; in contrast, LST withholding means "*passively allowing the patient to die*" [72]. However, consequentialists see no ethically relevant distinction, because the end-result of these practices is essentially the same [72]. Regarding palliative sedoanalgesia, current European guidelines are fairly explicit about indications and intensity of treatment (see above).

Addressing the issue of limited resources constitutes a major challenge in both developing and developed countries. Indeed, at global level, the equitable access to best possible emergency care [5] including expensive technological advancements such as extracorporeal CPR [64] seems like a theoretical ideal rather than a possible, near-future achievement. In sharp contrast, the widespread use of simple and beneficial interventions such as bystander CPR could be substantially augmented through organized, international education on resuscitation, preferably supported by the World Health Organization (WHO) and international Resuscitation Councils. WHO has already issued guidelines and launched initiatives to promote basic resuscitation of neonates in developing countries, thus improving accessibility to emergency care and potentially reducing subsequent morbidity/disability and/or mortality in this vulnerable population subgroup.

Regarding research, transparency could be promoted through data-sharing policies [73], and governmental funding of resuscitation research could be increased to become proportionate to cardiac arrest mortality burden [71]. Furthermore, the ethical credibility of partnerships between private and public sectors should be augmented by striking a balance between commercial interests and goals of investigators to promote science [74]. Lastly, patients/families might actively contribute to the development of research objectives and ethical/clinical practice guidelines.

Conclusion

Major challenges regarding the ethics of the rapidly advancing resuscitation science need to be addressed through widespread, coordinated, and sometimes resource-demanding interventions. The physical, ethical and wider societal impacts of such actions need to be supported by ongoing and future research.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-018-5202-0) contains supplementary material, which is available to authorized users.

Author details

[1] First Department of Intensive Care Medicine, National and Kapodistrian University of Athens Medical School, Evaggelismos General Hospital, 45-47 Ipsilandou Street, 10675 Athens, Greece. [2] Division of Health Sciences, Warwick Medical School, Gibbet Hill Campus, Coventry CV4 7AL, UK. [3] Acute Medicine, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK. [4] Istituto Anestesiologia e Rianimazione, Università Cattolica del Sacro Cuore Fondazione Policlinico, Universitario Agostino Gemelli, Largo Francesco Vito 1, 00168 Rome, Italy. [5] European University, Engomi, Cyprus. [6] President Hellenic Society of Cardiopulmonary Resuscitation, Athens, Greece. [7] University of Pittsburgh, Pittsburgh, PA 15260, USA. [8] Department of Emergency Medicine Oregon Health and Science University Portland, Center for Policy and Research in Emergency Medicine, Portland, OR, USA. [9] Department of Anesthesiology and Pain Therapy, University of Bern, Bern University Hospital, 3010 Bern, Switzerland. [10] Department of Intensive Care, Department of Ethics and Philosophy of Medicine, Erasmus MC University Medical Center, Rotterdam, The Netherlands. [11] Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium. [12] European Resuscitation Council, Niel, Belgium.

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Compliance with ethical standards

Conflicts of interest

Gavin Perkins has received research funding from the National Institute for Health Research to conduct studies in cardiac arrest; he holds volunteer roles within the Resuscitation Council (UK), European Resuscitation Council and International Liaison Committee on Resuscitation. Leo Bossaert holds volunteer roles within the European Resuscitation Council. Robert Greif holds a volunteer role within the European Resuscitation Council and International Liaison Committee on Resuscitation. No other author has a conflict of interest to disclose.

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