A Bayesian Perspective
Extracorporeal CPR for Refractory Out-of-Hospital Cardiac Arrest

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Abstract

A recent randomized clinical trial, INCEPTION, reported patients with refractory out-of-hospital cardiac arrest, extracorporeal CPR (eCPR) and conventional CPR (cCPR) had similar effects on survival with a favorable neurologic outcome. The current study examines if a Bayesian perspective provides additional insights. Depending on the prior selected, the Bayesian approach for the INCEPTION intention-to treat (ITT) analysis shows an equivalence probability between 13.4 - 16.8% (defined as 1 / 1.1 < odds ratio (OR) < 1.1). The probability of clinical superiority with eCPR ranges from 65.7 - 77.0 % (defined as OR > 1.1). A similar analyses using INCEPTION per protocol data shows an equivalence probability between 4.7 - 20.2% with reduced probabilities of clinical superiority of approximately 25%. It is concluded that a Bayesian perspective allows considerable additional insights into the trial analysis and interpretation. The substantial probabilities of increased survival, but with considerable residual uncertainties, suggests that additional studies are required before concluding that eCPR and cCPR have similar survival effects.

Keywords: extracorporeal CPR, Bayesian statistics

1. Introduction

Out-of-hospital cardiac arrest is a frequent event and fortunately its devastating consequences can be partially mitigated by rapid commencement of basic life support with high-quality chest compressions and external defibrillation (conventional cardiopulmonary resuscitation (CPR)). However, there remains a substantial subset of individuals who do not respond rapidly to these measures and whether more invasive measures. Whether the addition of more aggressive measure including extracorporeal CPR (the addition of extracorporeal membrane oxygenation to standard advanced cardiac life support (eCPR)) can improve survival and diminish anoxic brain injury is a current topic of research. The largest randomized clinical trial (RCT) examining this question recently published their results[1]. For the primary outcome, 30 day survival without significant neurological deficit, the authors observed an odds ratio of 1.4 (95% confidence interval, 0.5 to 3.5; P = 0.52) in favor of extracorporeal CPR for leading to their conclusion "In patients with refractory out-of-hospital cardiac arrest, extracorporeal CPR and conventional CPR had similar effects on survival with a favorable neurological outcome".[1]

This communication does not reiterate the many reasons to be wary of null hypothesis significance testing (NHST), p values and confidence intervals[2]. Rather it assumes the reader has perhaps heard that Bayesian methods mirror our intuitive learning and diagnostic processes and is curious about its potential application to RCT analyses and interpretations.

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4. Tables

Table 1 Extracted ITT trial data

Trial	Fail CPR (n)	Fail eCPR (n)	Success CPR (n)	Success eCPR (n)
INCEPTION	52	56	10	14
ARREST	15	8	0	6
PRAGUE	108	86	24	38

eCPR = extracorporeal cardiopulmonary resuscitation

Table 2 eCPR odds ratios, 95% credible intervals and probabilities with various priors

Priors	OR	95% CrI		Probabilities		
	point estimate	lower limit	upper limit	p(OR) >1	p(OR) >1.1	p(ROPE)
Vague	1.32	0.543	3.21	0.727	0.657	0.134
Combined	1.35	0.705	2.58	0.817	0.732	0.153
Enthusiastic	1.40	0.738	2.67	0.849	0.770	0.138
Skeptical	1.32	0.700	2.50	0.804	0.710	0.168

Vague: default vague prior
Combined: prior eCPR data from ARREST + PRAGUE
Enthusiastic: prior eCPR data from ARREST alone
Skeptical: prior eCPR data from PRAGUE alone
ROPE: range of practical equivalence = + / - 10% OR (odds ratio)

Table 3 eCPR (per protocol) odds ratios, 95% credible intervals and probabilities with various priors

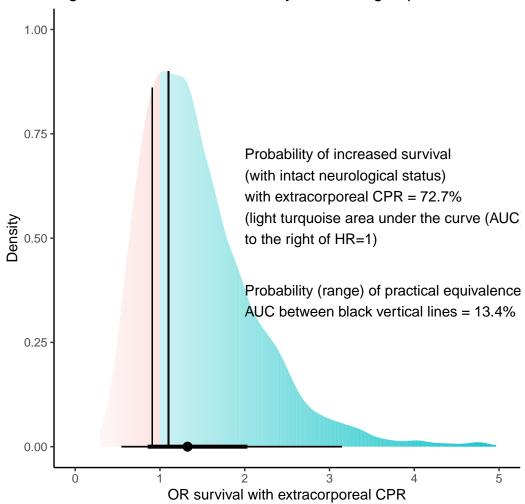| Priors	OR	95% CrI		Probabilities		
	point estimate	lower limit	upper limit	p(OR) >1	p(OR) >1.1	p(ROPE)
Vague	0.451	0.151	1.35	0.0698	0.0488	0.0473
Combined	0.859	0.430	1.71	0.33	0.2380	0.2022
Enthusiastic	0.870	0.437	1.73	0.345	0.2512	0.2013
Skeptical	0.858	0.419	1.75	0.327	0.2370	0.1970

Vague: default vague prior
Combined: prior eCPR data from ARREST + PRAGUE
Enthusiastic: prior eCPR data from ARREST alone
Skeptical: prior eCPR data from PRAGUE alone
ROPE: range of practical equivalence = + / - 10% OR (odds ratio)

Figure 1 INCEPTION ITT analysis with vague prior

Probability of increased survival
(with intact neurological status)
with extracorporeal CPR = 72.7%
(light turquoise area under the curve (AUC)
to the right of HR=1)

Probability (range) of practical equivalence
AUC between black vertical lines = 13.4%

OR survival with extracorporeal CPR

Clinical superiority = AUC to right of vertical line at HR = 1.1 = 65.7%
thin horizontal line at 0 = 95% CrI with black circle = point estimate
thick horizontal line = +/− 68% CrI