Is the Statistical Deck Stacked in Observational Resuscitation Studies?

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Disclosure

- Chief Medical Advisor Stryker Emergency Care

Resuscitation Time Bias in Observational Resuscitation Studies

Andersen LW, Grossestreuer AV, Donnino MW. "Resuscitation time bias"-A unique challenge for observational cardiac arrest research. *Resuscitation*. 2018;125:79-82.


HAVE YOU TRIED
ACCEPT HYPOTHESIS
MAKE AN OBSERVATION
REJECT HYPOTHESIS
TRY AGAIN. BACK 2 STEPS
Scientific Method
ASK A QUESTION
?
CONDUCT AN EXPERIMENT
SUCCESS? FORWARD 2 STEPS
FORM A HYPOTHESIS
The Scientific Method?

Pathways to Scientific Knowledge

- Randomized clinical trials: formerly constructed to answer a clinical question by controlling variables and having enough data to reach a conclusion that has statistical significance. Commonly used to show a causal relationship between the use of a drug or device and a clinical outcome
- Observational trials: study A type of study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome. There can be associations of interventions and outcomes but cannot show causality

Types of bias in observational studies

- Selection bias: selection of individuals, groups or data for analysis in such a way that proper randomization is not achieved, thereby ensuring that the sample obtained is not representative of the population intended to be analyzed
- Information bias: results from wrong or inexact recording of individual factors
- Confounding: a risk factor for the disease under study is associated with the exposure of interest but is not causal
- Immortal

Resuscitation Time Bias

- A unique situation in which an exposure is more likely to occur the longer the cardiac arrest continue. Since length of resuscitation is strongly associated with worse outcomes, this will bias the result toward a harmful effect of the exposure

Resuscitation Time Bias

- Pertains to observational studies of exposures (e.g. drugs, airway management)
- An exposure is more likely to occur the longer the cardiac arrest continues.
- Length of resuscitation is strongly associated with worse outcome, tends to bias the results toward a harmful effect
- This bias is the reverse of immortal time bias

Resuscitation Time Bias

- Interventions that occur intra-cardiac arrest related to time:
  - Interventions are more likely to be implanted the longer the duration of the cardiac arrest
  - Once ROSC is achieved or cardiac arrest is terminated without ROSC, the interventions cannot be performed
  - These interventions may result in ROSC thereby shortening the duration of arrest

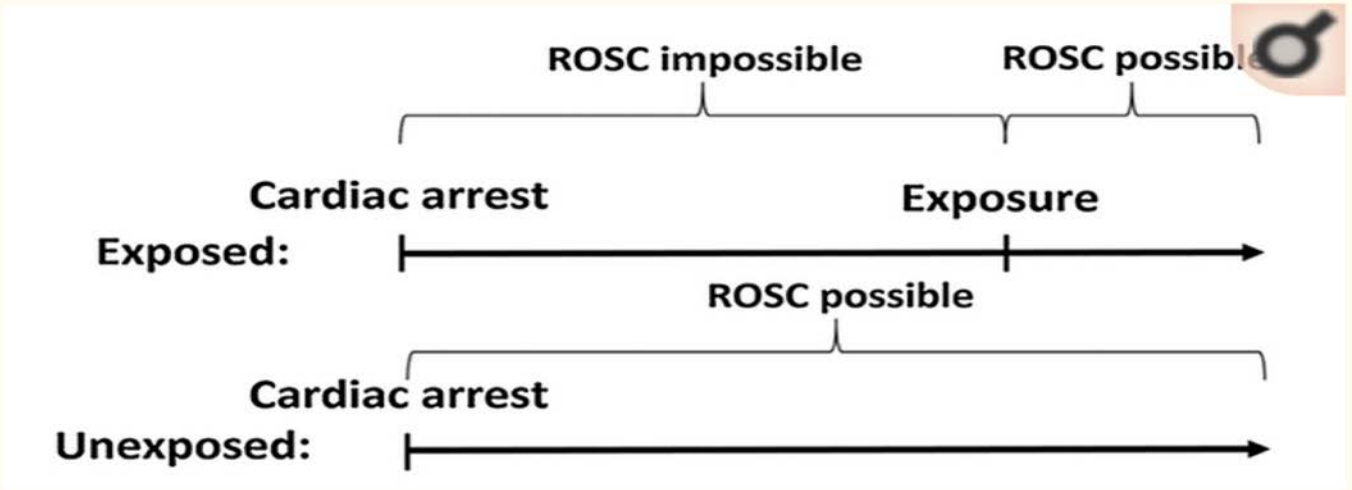


Fig. 2.

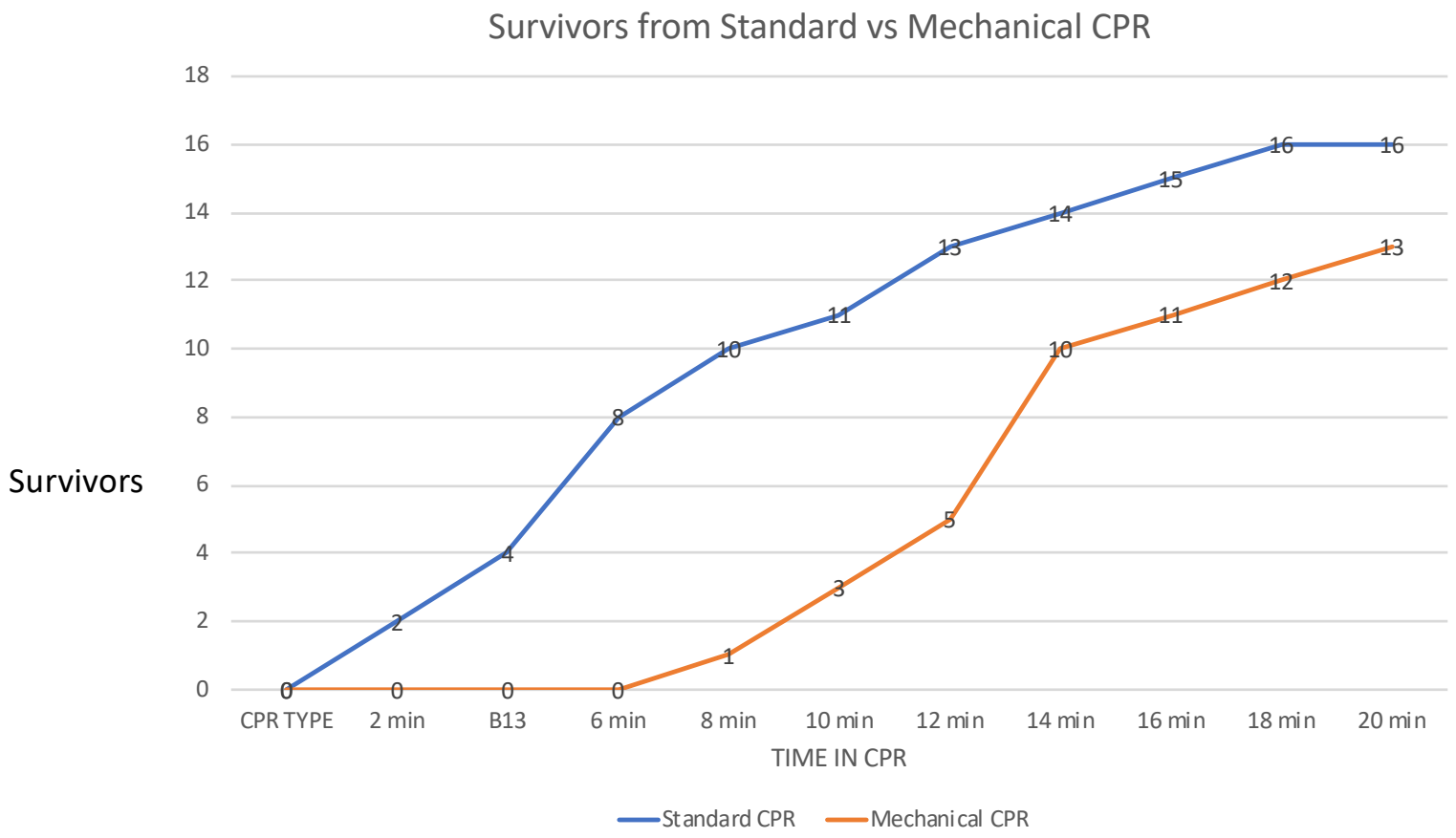
Resuscitation time bias. Graphical example illustrating resuscitation time bias. Due to the way the exposure is defined, patients in the exposed group have longer cardiac arrest. Since longer cardiac arrests are associated with poor outcomes, this artificially favors the unexposed group, biasing the results.

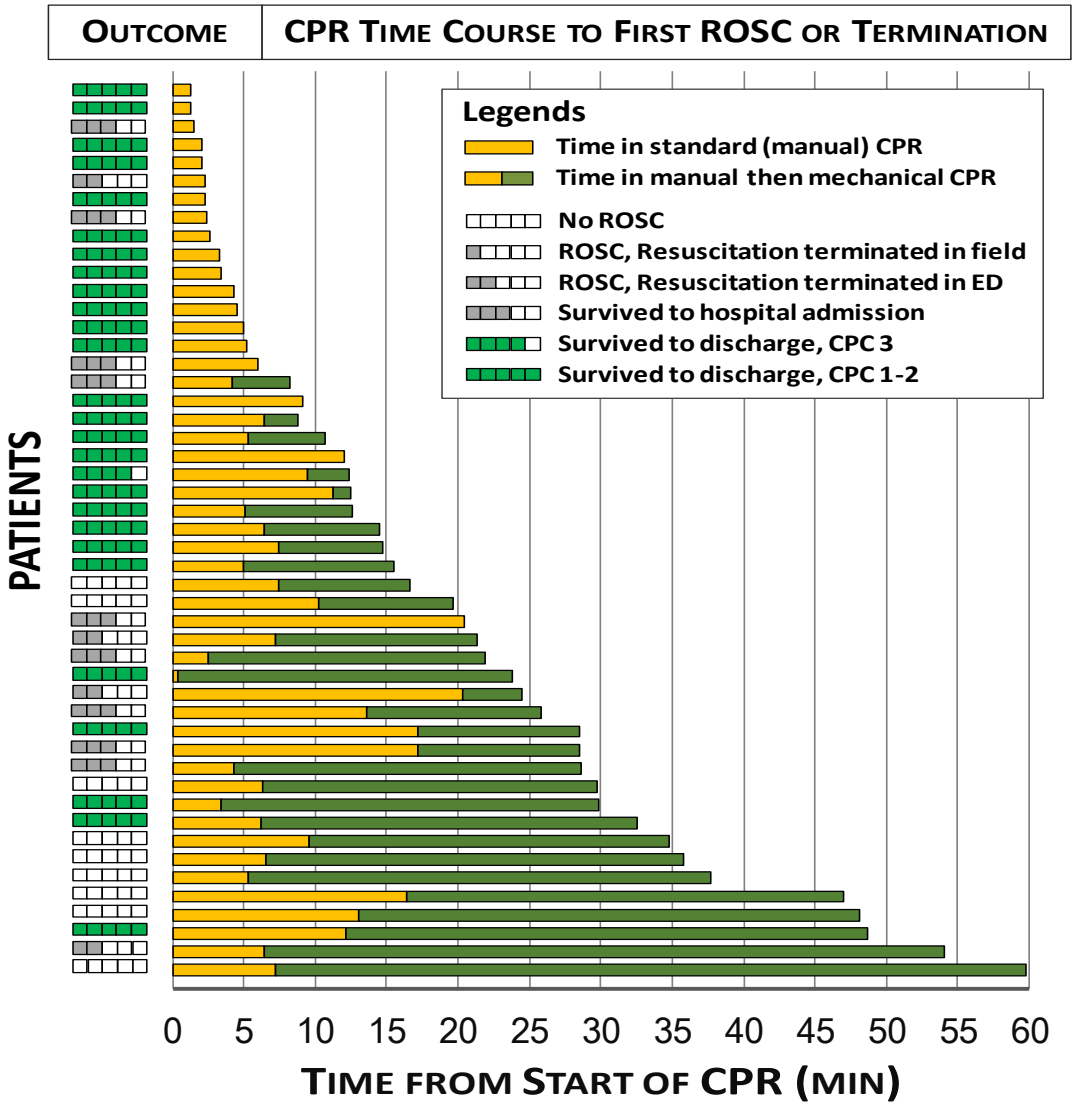
Example

- Japanese study 2012 examined association between epinephrine administration and outcomes of OHCA.
  - Did not adjust for timing of epinephrine administration (likely to occur late)
  - Worse survival was found
- A second study with same data adjusted for time of administration
  - Their results showed favorable outcome more likely with epinephrine for both shockable (OR 1.36 95% CI: 1.13,1.63) and nonshockable OR 1.78 95/5 CI: 1.49,2.13)

Outcome parameters (N (%))	All (N= 49)	sCPR (N = 19)	mCPR (N = 30)	P-value
ROSC anytime	40 (82%)	19 (100%)	21 (70%)	0.008
Survived to hospital admission, all VF/VT	36 (73%)	18 (95%)	18 (60%)	0.008
Good cerebral performance, CPC 1	23 (47%)	13 (68%)	10 (33%)	0.021
Moderate disability, CPC 2	3 (6%)	1 (5%)	2 (7%)	>0.99
Severe disability, CPC 3	1 (2%)	0 (0%)	1 (3%)	>0.99

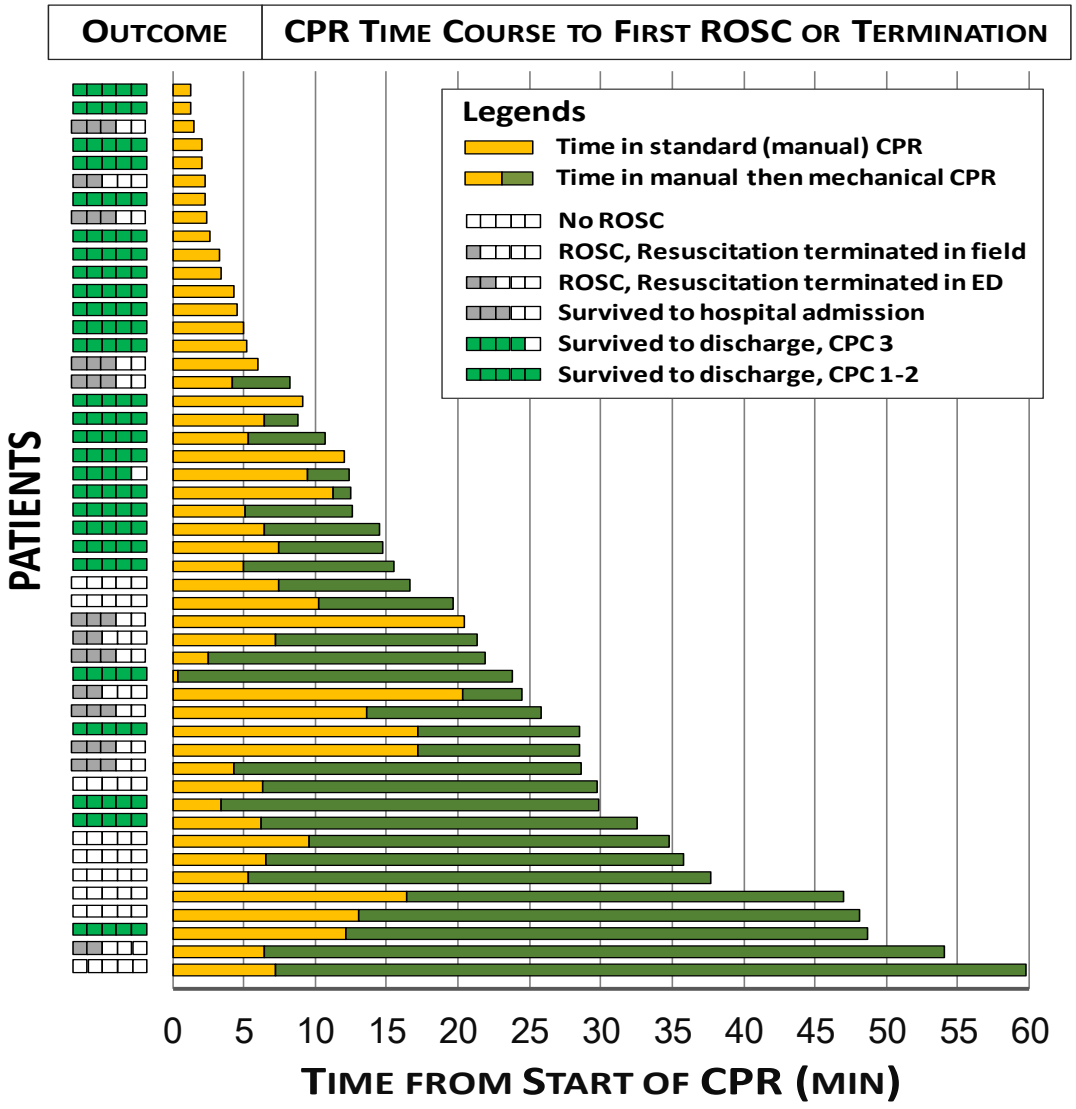
sCPR = standard manual-only CPR, mCPR = manual transitioning to mechanical CPR, ROSC = Return Of Spontaneous Circulation, CPC = Cerebral Performance Category,


Survivors from Standard vs Mechanical CPR
Survivors
18
16
14
12
10
8
6
4
2
0
0
2
4
8
10
11
13
14
15
16
16
0
0
0
0
1
3
5
10
11
12
13
CPR TYPE
2 min
B13
6 min
8 min
10 min
12 min
14 min
16 min
18 min
20 min
TIME IN CPR
Standard CPR
Mechanical CPR


OUTCOME
CPR TIME COURSE TO FIRST ROSC OR TERMINATION
Legends
Time in standard (manual) CPR
Time in manual then mechanical CPR
No ROSC
ROSC, Resuscitation terminated in field
ROSC, Resuscitation terminated in ED
Survived to hospital admission
Survived to discharge, CPC 3
Survived to discharge, CPC 1-2
PATIENTS
0 5 10 15 20 25 30 35 40 45 50 55 60
TIME FROM START OF CPR (MIN)

Resuscitation Time Bias

Odds of Success Low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PATIENTS
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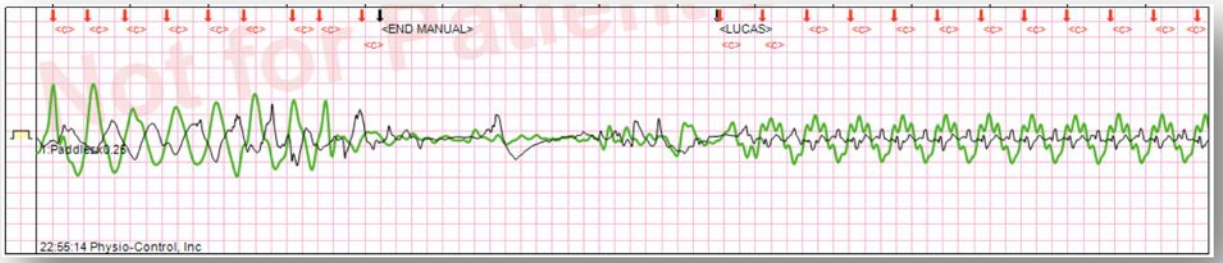
TIME FROM START OF CPR (MIN)

Require Time Data!!



Conclusions

- Resuscitation research is hard!
- Observational studies are convenient and can yield helpful information
- Controlling variables by cohort matching implies that we know all of the variable
- Be VERY skeptical of observational studies looking at an intervention such as device or drug IF TIME of EXPOSURE is not specifically listed

Thank you

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