INSTITUT
JULES BORDET

La réanimation cardiorespiratoire

Support vital en soins intensifs oncologiques

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Why to talk about that ?

- The appropriateness of CPR in cancer patients is an important clinical and ethical issue.
- Survival after cardiac arrest (CA) remains low despite major advances in management during resuscitation and after the return of spontaneous circulation (ROSC).
- Few data available on survival rates in patients with malignancies.
- Substantial improvements in the survival of patients with malignancies admitted to the ICU have been achieved in recent years but cancer patients are still considered as poor candidates to ICU admission.

Cardiopulmonary resuscitation (CPR) and malignancy

CPR overall hospital survival

- ~10% after out-of-hospital cardiac arrest (OHCA).
- Intra hospital CA (IHCA):
  - 200000 adults/year in USA
  - Survival: [10 – 20] %.
- From 2000 to 2014: survival to discharge increased from 14% to 25%.

Malignancy

- 2nd leading cause of death globally.
- 9.6 million deaths in 2018.
- 25.4% of all deaths in EU.
- Overall cancer death rate has declined since the early 1990s.

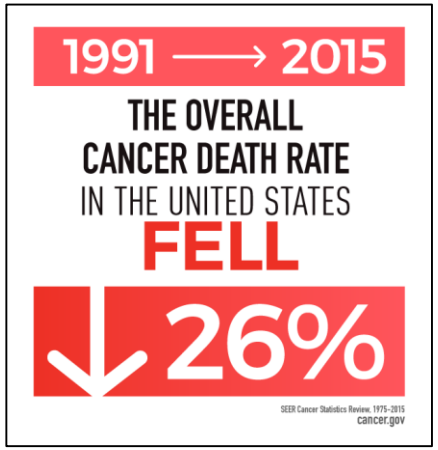
WHO, 2019

U.S. Cancer Mortality Trends

In the United States, the overall cancer death rate has declined since the early 1990s.

The most recent SEER* Cancer Statistics Review, released in April 2018, shows that cancer death rates decreased by:

- 1.8% per year among *men* from 2006 to 2015
- 1.4% per year among *women* from 2006 to 2015
- 1.4% per year among *children* ages 0–19 from 2011 to 2015.



* The Surveillance, Epidemiology, and End Results (SEER)

Cardiopulmonary resuscitation (CPR) and malignancy

- Cancer survivors have increased rates of major cardiovascular events (including IHCA) with poorer outcomes.

- Many of these patients carry diagnoses of highly-treatable or non-advanced cancers (ex. breast or prostate cancers), suggesting that patients with cancer may be under-resuscitated.

- It is reasonable to postulate that cancer patients, particularly those free of advanced disease, should share similar resuscitation rates compared to cancer-free patients.

Champigneuille et al. Resuscitation 2015

Effectiveness of Cardiopulmonary resuscitation

Support Care Cancer. 1993 May;1(3):135-8.

Cardiopulmonary resuscitation in medical cancer patients: the experience of a medical intensive-care unit of a cancer centre.

Sculier JP[1], Markiewicz E.

- Retrospective analysis of ICU patients – 6-years period
- 49 ARCA non surgical cancer patients
- 19 (39%) → Successful CPR
- 5 (10%) → Discharged alive from hospital

Successful CPR in 8 patients with acute cardiovascular drug toxicity

Table 2 Results of cardiopulmonary resuscitation (*CPR*) according to patients' clinical characteristics in a medical oncology intensive-care unit (*ICU*) [78]. *Category A* patients who failed to respond to CPR, *category B* patients who had successful CPR but died later in the ICU, *category C* patients who had successful CPR but died in the hospital after discharge from the ICU, *category D* patients who had successful CPR and were discharged from the hospital

	Category			
	A	B	C	D
n	30	12	2	5
Mean age (years)	50	56	57	52
Range	20–77	26–77	54–60	42–63
Type of tumour				
Solid	13	7	2	5
Locoregional	3	2	—	1
Metastatic	10	5	2	4
Haematological	17	5	—	—
Functional stage				
Diagnosis	2	—	—	—
Treatment for cure	14	4	—	—
Treatment for control	11	5	1	5
Candidate for palliative care	3	3	1	—
Cause of admision to ICU				
Cardiac arrest	5	5	2	2
Anticancer treatment	—	—	—	3
Medical complications	25	7	—	—
Cause of cardiac arrest				
Drug cardiovascular toxicity	—	2	1	5
Other causes	30	10	1	0

Effectiveness of Cardiopulmonary resuscitation

Vitelli et Al. 1991

- 3-years period
- ARCA: 750 patients / 114 cancer patients
- 75 (66%) → ROSC
- 12 (16%) → Hospital discharge
  - Overall mean survival after discharge: 223 days (median:150 days; range: 3-350 days)

Performance Status: the single significant independent factor predicting the discharge from hospital after ARCA.

Age, interval between cancer diagnosis and ARCA, sex, underlying malignancy, cause of arrest were not significant.

Table 1 Prognostic factors after cardiopulmonary resuscitation in cancer patients

Studies	Study population	Survival rate to discharge								
		Overall (%)	Subgroups							
			Karnofsky <50 vs. >50 %	Localized vs. metastatic disease	Solid vs. hematologic malignancy[a]	Lymphoma/ myeloma vs. leukemia vs. HSCR	Unanticipated vs. anticipated arrest	Location: in-patient floor vs. ICU	Metastatic malignancy	Hematologic malignancy
Vitelli, [15]	$n = 114$ IHA	10.5	2.3 vs. 17.5 % ($p = 0.018$)	–	–	–	–	13 vs. 6 % ($p > 0.05$)	–	9 % ($n = 44$)
Varon, [12]	$n = 83$ IHA	9.6	–	–	–	–	–	–	–	–
Ewer, [14]	$n = 244$ IHA	6.6	–	–	12.3 vs. 1.5 % ($p = 0.001$)	–	21.9 vs. 0.0 % ($p < 0.001$)	13.7 vs. 1.4 % ($p < 0.001$)	–	–
Reisfield [11]	$n = 1707$ IHA	6.2	–	9.5 vs. 5.6 % ($p = 0.05$)	7.1 vs. 2.0 % ($p = 0.001$)	3.4 vs. 0.9 vs. 0.0 % ($p = 0.027$-2)	–	10.1 vs. 2.2 % ($p < 0.001$)	–	–
Hwang, [7]	$n = 41$ OOHA	4.9	–	–	–	–	–	–	–	–
Ebell, [1]	$n = 4267$ IHA	6.6	–	–	–	–	–	–	1.9 % ($n = 1326$)	1.3 % (n = 554)

IHA in-hospital arrest, *OOHA* out-of-hospital arrest, *Karnofsky* Karnofsky performance status, *HSCR* hematopoietic stem cell recipients, *ICU* intensive care unit

[a] Including myeloma, lymphoma, leukemia, and hematopoietic stem cell recipients

How many ROSC?

- Between 1 Jan 1993 and 31 Dec 1994
- 83 IHCA patients received CPR; 42♀.
- Mean age: 56.2 years.

- Type of cancer:
  - 42% hematologic malignancy.
  - 58% solid cancer.
    -19% lung,
    -15% gastrointestinal,
    -5% head and neck
    -19% other malignancies.

Should a cancer patient be resuscitated following an in-hospital cardiac arrest?

Joseph Varon [a,*], Garrett L. Walsh [b], Paul E. Marik [c], Robert E. Fromm [a,d]

[a] *Pulmonary and Critical Care Section, Baylor College of Medicine, Department of Emergency Services, The Methodist Hospital, 6565 Fannin M 196, Houston, TX 77030, USA*
[b] *Department of Thoracic and Cardiovascular Surgery, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*
[c] *Department of Medicine, University of Massachusetts, Medical Intensive Care Unit, St. Vincent Hospital, Worcester, MA 01640, USA*
[d] *Cardiology Section, Baylor College of Medicine, Department of Emergency Services, The Methodist Hospital, 6565 Fannin M 196, Houston, TX 77030, USA*

Results

- 31/83 (33.7%) had no ROSC.
- 52/83 (66.3%) had ROSC.

- 44/52 (84%) died in hospital.

Excellent ROSC following a cardiac arre

Survival to discharge: subgroups analysis

Survival in cancer patients undergoing in-hospital cardiopulmonary resuscitation: A meta-analysis☆

Gary M. Reisfield[a,*], Susannah Kish Wallace[b,1], Mark F. Munsell[c,2], Fern J. Webb[d,3], Edgar R. Alvarez[e,4], George R. Wilson[e,5]

- 47 studies between 1966 and August 2005 identified, 42 studies included.
- 1707 patients met the inclusion criteria.

Table 2 Percent of survivors to hospital discharge and 95% confidence intervals for subgroups of patients who underwent in-hospital cardiopulmonary resuscitation

	Number of survivors/ number of patients	Percent of survivors	95% Confidence interval
Solid tumor	51/718[a]	7.1	3.3–10.9
Localised	28/295	9.5	4.3–14.6
Metastatic	23/411	5.6	1.4–8.6
Hematologic/HSCT recipients	8/400[a]	2.0	0–4.4
Lymphoma/myeloma	2/59	3.4	0–6.9
Leukemia	2/219	0.9	0–3.0
HSCT recipients	0/56	0.0	–
Location of arrest			
Intensive Care Unit	11/500	2.2	0–4.6
Ward	18/179	10.1	3.5–16.6
Time period			
Pre-1990	12/324	3.7	0–7.9
1990–2005	93/1383	6.7	3.0–10.4

HSCT: hematopoietic stem cell transplantation.
[a] Numerator and denominator totals exceed that of the subgroups because some studies did not stratify according to subgroup.

Resuscitation (2006) **71**, 152—160

Survival to discharge → 6.2%

- Solid tumor 7.1%
  - Localised 9.5% Vs Metastatic 5.6%
- Hematologic 2%
- ICU 2.2% Vs Ward 10.1%
- Pre-1990: 3.7% Vs 1990-2005: 6.7%

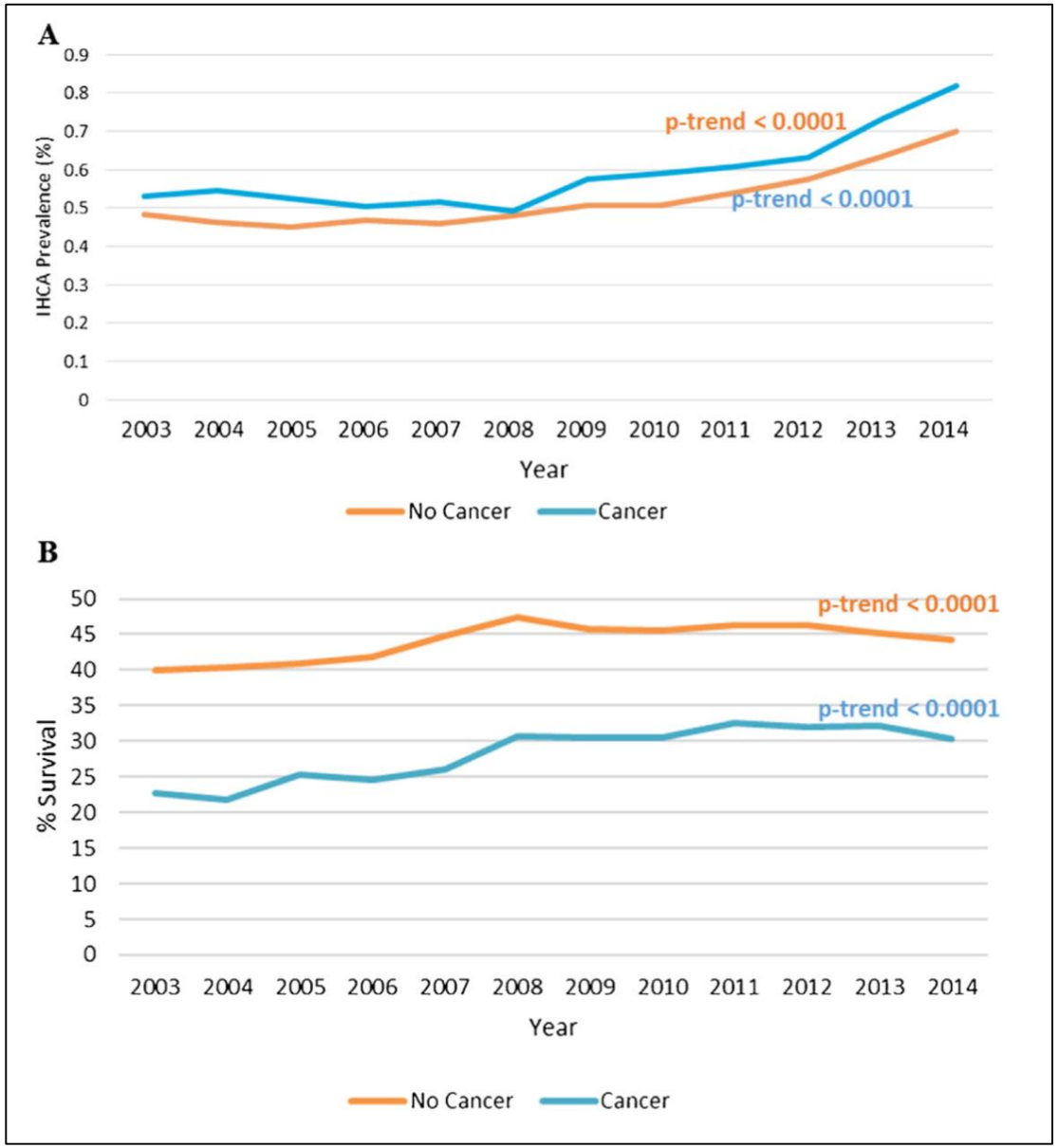
Survival in unselected patients 10-20%

Clinical paper

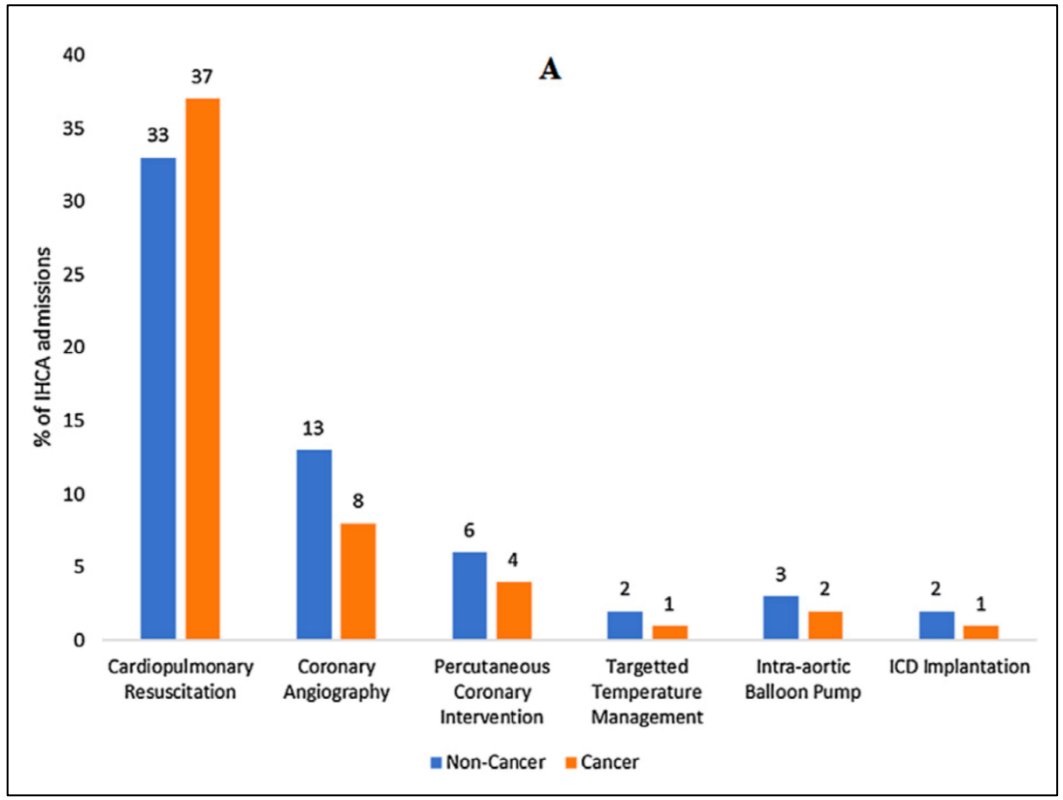
Contemporary impacts of a cancer diagnosis on survival following in-hospital cardiac arrest

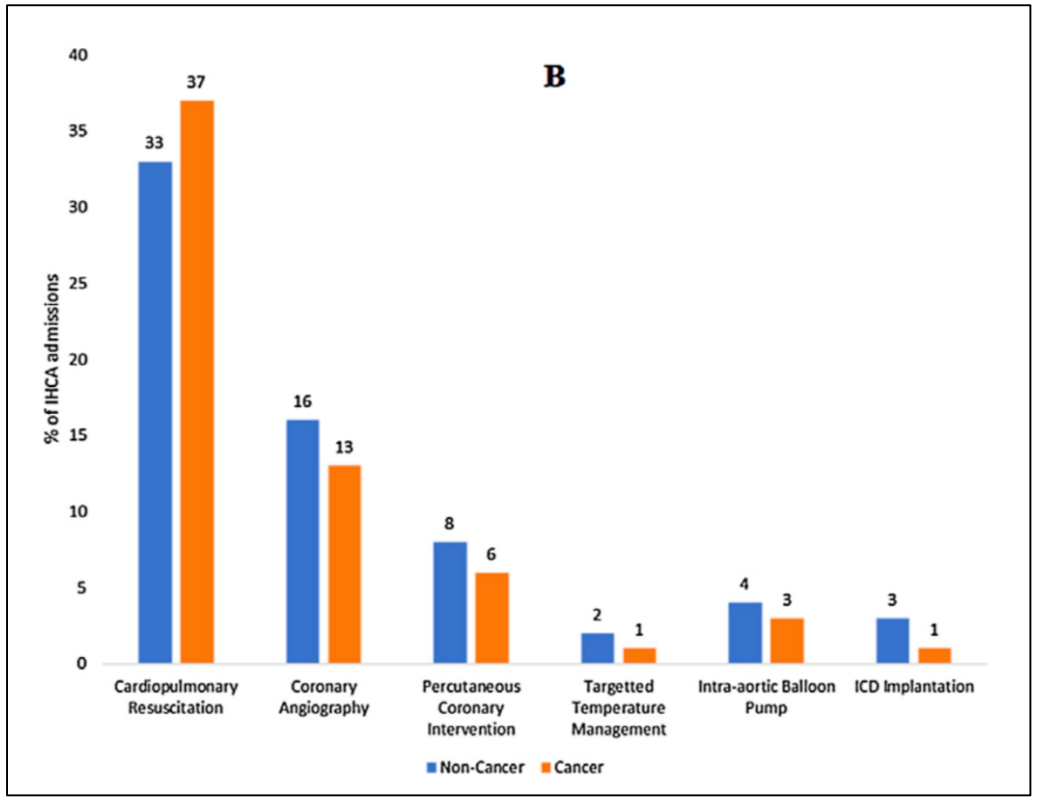
Avirup Guha[a,b,1], Benjamin Buck[a,1], Michael Biersmith[a], Sameer Arora[c,d], Vedat Yildiz[e], Lai Wei[e], Farrukh Awan[f], Jennifer Woyach[f], Juan Lopez-Mattei[g,h], Juan Carlos Plana-Gomez[i], Guilherme H. Oliveira[b], Michael G. Fradley[j], Daniel Addison[a,]*

- 1 893 768 admissions complicated by IHCA from 2003 to 2014.
- The annual rate of IHCA increased in both groups over the study periods (p < 0.0001).
- Survival to hospital discharge improved in both groups:
  - 22.6% → 30.2% in cancer patients Vs
  - 40.2% → 45.1% in non-cancer patients (p<0.0001).



What about after-CPR ?





Procedural utilization within 2012-2015 cohort.
All P-values < 0.001

Guha et al. Resuscitation 142(2019)30–37

Subjects with a generally favourable 5-years survival:

- Angiography: P = 0.0337
- PCI: P = 0.0151
- ICD implantation: P – 0.008

What about after-CPR ?

Patterns of Resuscitation Care and Survival After In-Hospital Cardiac Arrest in Patients With Advanced Cancer

Jeffrey T. Bruckel, Sandra L. Wong, Paul S. Chan, Steven M. Bradley, and Brahmajee K. Nallamothu

- Retrospective study, Get With The Guidelines – Resuscitation registry.
- 47,157 adults non-surgical patients with IHCA, 369 hospitals, from April 2006 to June 2010.
- Rates of ROSC and survival to discharge between *Advanced Cancer* and *Non Cancer* patients.
- Advanced cancer is defined as the presence of metastatic or hematologic malignancy.

Table 2. Unadjusted Survival Rates, Unadjusted Relative Risk for Survival by Cancer Status, Multivariate-Adjusted Survival by Cancer Status, and DNAR Status for Patients With and Without Cancer

Outcome	No Cancer	Cancer	RR (95% CI)	*P*
ROSC				
Unadjusted, % (No.)	63.0 (25,545)	57.5 (3,784)	0.91 (0.89 to 0.93)	< .001
Adjusted*, % (95% CI)	56.6 (53.8 to 59.5)	52.3 (49.5 to 55.3)	0.93 (0.90 to 0.95)	< .001
Survival to discharge				
Unadjusted, % (No.)	19.2 (7,796)	9.6 (635)	0.50 (0.45 to 0.54)	< .001
Adjusted*, % (95% CI)	13.4 (12.1 to 14.8)	7.4 (6.6 to 8.4)	0.55 (0.51 to 0.60)	< .001
Overall DNAR status				
Unadjusted rates, % (No.)	43.0 (10,974)	55.6 (2,103)	1.29 (1.25 to 1.34)	< .001
Adjusted* rates, % (95% CI)	41.6 (40.3 to 43.1)	50.4 (48.4 to 52.5)	1.21 (1.17 to 1.25)	< .001
DNAR < 48 hours after arrest				
Unadjusted rates, % (No.)	27.1 (6,920)	37.3 (1,411)	1.38 (1.31 to 1.44)	< .001
Adjusted* rates, % (95% CI)	25.5 (24.4 to 26.6)	33.2 (31.4 to 35.1)	1.30 (1.24 to 1.37)	< .001
DNAR > 48 hours after arrest				
Unadjusted rates, % (No.)	13.5 (3,451)	14.6 (554)	1.08 (1.00 to 1.18)	.060
Adjusted* rates, % (95% CI)	12.6 (12.0 to 13.3)	12.6 (11.4 to 13.8)	1.00 (0.91 to 1.09)	.930

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- Patients with cancer had a higher rate of conversion to DNAR status within the first 48 hours after the arrest.

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Resuscitation Quality

Knowledge of a patient's underlying disease process and anticipated prognosis could potentially influence the resuscitation effort .

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JT Bruckel et al 2017

Table 3. Resuscitation Quality Measures for Patients With and Without Cancer

Measurement	No Cancer	Cancer	RR of Failure (95% CI)	*P*
Duration of resuscitation (nonsurvivors), minutes				
Unadjusted mean (95% CI)	24.2 (23.9 to 24.6)	22.5 (21.7 to 23.3)	—	< .001
Adjusted* mean (95% CI)	24.1 (23.5 to 24.7)	22.5 (21.5 to 23.5)	—	< .001
Chest compressions, overall				
Unadjusted rates, % (No.)	98.5 (39,972)	99.4 (6,546)	0.40 (0.29 to 0.55)	< .001
Chest compressions within 2 minutes				
Unadjusted rates, % (No.)	96.4 (38,464)	97.5 (6,310)	0.70 (0.60 to 0.82)	< .001
Missing times, % (No.)	1.7 (689)	1.7 (114)	1.02 (0.84 to 1.24)	.850
Adjusted* rates, % (95% CI)	97.1 (96.5 to 97.6)	97.5 (96.9 to 98.0)	0.86 (0.74 to 0.99)	.030
Defibrillation for VT or VF patients, overall				
Unadjusted rates, % (No.)	91.2 (13,548)	91.6 (1,831)	0.96 (0.82 to 1.12)	.580
Adjusted rates, % (95% CI)	90.0 (86.8 to 92.4)	90.7 (87.3 to 93.1)	0.93 (0.80 to 1.09)	.400
Defibrillation for VT or VF patients, within 2 minutes				
Unadjusted rates, % (No.)	80.7 (11,629)	83.0 (1,598)	0.88 (0.79 to 0.98)	.010
Missing times, % (No.)	3.0 (438)	3.7 (74)	1.26 (0.99 to 1.60)	.070
Adjusted rates, % (95% CI)	77.3 (74.4 to 79.9)	79.8 (76.6 to 82.5)	0.89 (0.81 to 0.98)	.020
Adrenaline (epinephrine) for non-VT and non-VF patients, overall				
Unadjusted rates, % (No.)	90.8 (23,353)	92.7 (4,251)	0.79 (0.71 to 0.89)	< .001
Adjusted rates, % (95% CI)	90.7 (89.3 to 91.9)	92.3 (90.9 to 93.5)	0.82 (0.74 to 0.92)	< .001
Adrenaline (epinephrine) for non-VT and non-VF patients, within 5 minutes				
Unadjusted rates, % (No.)	80.0 (19,144)	81.6 (3,500)	0.92 (0.86 to 0.99)	.020
Missing times, % (No.)	7.0 (1,788)	6.4 (294)	0.92 (0.82 to 1.04)	.180
Adjusted rates, % (95% CI)	80.0 (77.9 to 81.9)	81.8 (79.6 to 83.8)	0.91 (0.86 to 0.97)	.004

JT Bruckel et al 2017

Quality of life at discharge

Should a cancer patient be resuscitated following an in-hospital cardiac arrest?

Joseph Varon [a,*], Garrett L. Walsh [b], Paul E. Marik [c], Robert E. Fromm [a,d]

[a] *Pulmonary and Critical Care Section, Baylor College of Medicine, Department of Emergency Services, The Methodist Hospital, 6565 Fannin M 196, Houston, TX 77030, USA*
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[d] *Cardiology Section, Baylor College of Medicine, Department of Emergency Services, The Methodist Hospital, 6565 Fannin M 196, Houston, TX 77030, USA*

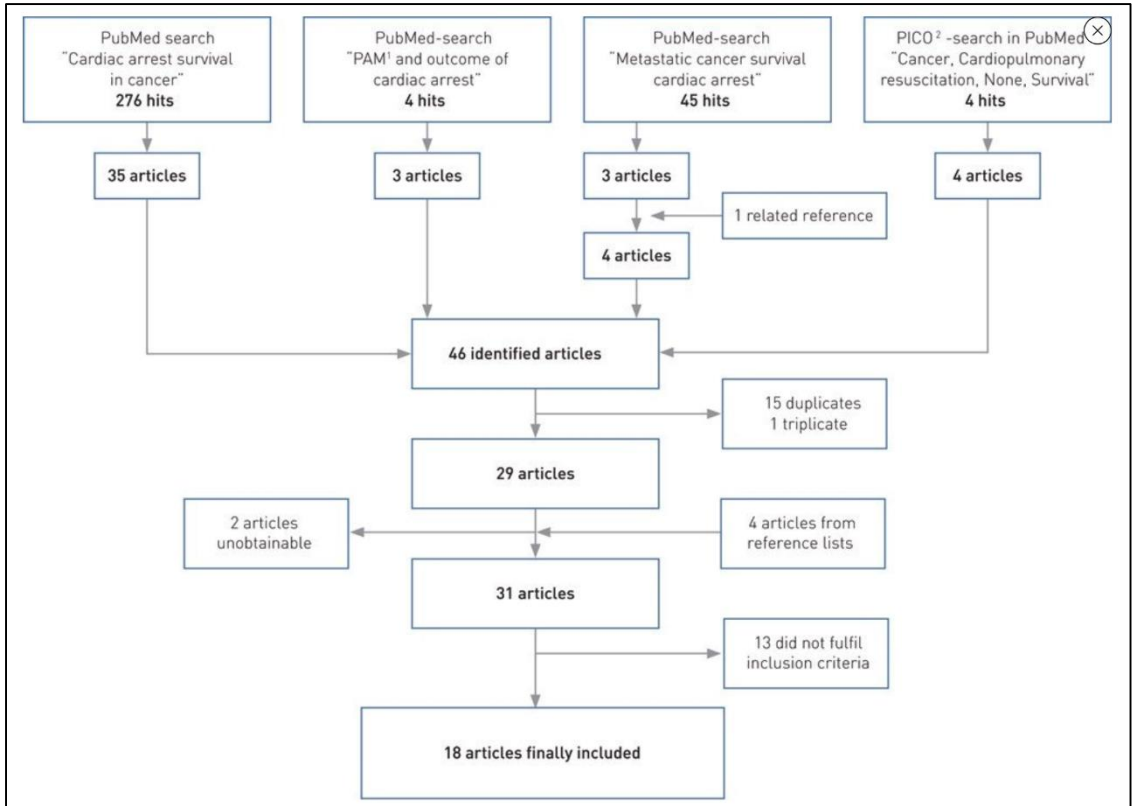
- 8/83 (9.6%) patients survived to hospital discharge.
- 3 patients were discharged to hospice care where they died within 6 weeks of discharge.
- 2 patients died within 6 months of hospital discharge.
- **3 (3.6%) patients survived to 1 year: two with ZFS* 1 and one with ZFS 2.**

*ZFS: Zubrod fuctional's status

When to consider CPR to be futile?

Cardiopulmonary resuscitation in palliative care cancer patients

Odd Jarle Kjørstad, Dagny Faksvåg Haugen About the authors



Flow chart for literature searches and selection of articles

Exclusion criteria:

- age under 18
- language other than English.

Table 2 Post-CPR survival rate in different studies, review articles and meta-analyses

Patient group	First author, year published (reference)	Type of study/article	Number of patients	Return of spontaneous circulation (%)	Discharged alive (%)
Unselected patients	George, 1989 (8)	Clinical study	140		24.3
	Ballew, 1994 (15)	Clinical study	313		16.0
	Hamill, 1995 (23)	Review article			15
	Ebell, 1998 (13)	Meta-analysis	9 398	43.1	14.6
	Varon, 2007 (27)	Review article		31	15
	Larkin, 2010 (17)	Cohort study	49 130		17.4
Cancer patients, undifferentiated	Vitelli, 1991 (20)	Clinical study	114	65.8	10.5
	Ebell, 1992 (12)	Meta-analysis	276		5.8
	Ebell, 1998 (13)	Meta-analysis	3 733		6.7
	Varon, 1998 (19)	Clinical study	83	66.3	9.6
	Ewer, 2001 (16)	Clinical study	243		6.6
	Wallace, 2002 (21)	Clinical study	406	37	2
	Reisfield 2006 (14)	Meta-analysis	1 707		6.2
Cancer patients, localised disease	Reisfield 2006 (14)	Meta-analysis	295		9.5
Cancer patients, metastatic disease	Ebell, 1992 (12)	Meta-analysis	141		0
	Dautzenberg, 1993 (22)	Review article			0
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When should CPR not be administered?

Cardiopulmonary resuscitation in palliative care cancer patients

Odd Jarle Kjørstad, Dagny Faksvåg Haugen About the authors

CPR will be unsuccessful in patients with:

- terminated tumor-directed treatment
- extensive metastasis
- performance status poorer than WHO score 2.

CAN THE OUTCOME BE PREDICTED?

Table 1 Pre-Arrest Morbidity Index (PAM index) for use in predicting the results of cardiopulmonary resuscitation in unselected patient groups (8). The score is the sum of the numerical values of the factors shown.

PAM index factors	Numerical value
Hypotension, systolic pressure < 90 mm Hg	3
Renal failure; S-creatinine > 220 micromol/L	3
Malignancy	3
Pneumonia	3
Homebound lifestyle	3
Angina pectoris	1
Heart failure, NYHA class III and IV	1
Acute MI	1
S3 gallop rhythm	1
Oliguria, urine production < 300 ml/24 h	1
Sepsis	1
Mechanical ventilation	1
Recent cerebrovascular event	1
Coma	1
Cirrhosis of the liver	1

Karnofsky Scale		Zubrod Scale	
Normal, no evidence of disease Able to perform normal activity with only minor symptoms	100 90	Normal activity	0
Normal activity with effort, some symptoms Able to care for self but unable to do normal activities	80 70	Symptomatic and ambulatory Cares for self	1
Requires occasional assistance, cares for most needs Requires considerable assistance	60 50	Ambulatory >50% of time Occasional assistance	2
Disabled, requires special assistance Severely disabled	40 30	Ambulatory ≤50% of the time Nursing care needed	3
Very sick, requires active supportive treatment Moribund	20 10	Bedridden	4

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Mechanical ventilation	1
Recent cerebrovascular event	1
Coma	1
Cirrhosis of the liver	1

- The PAM index was considered in several studies of unselected patients.
- There were no survivors with a PAM index > 8 in this metanalysis.
- *Dautzenberg et al*. recommend reducing the weighting in the PAM index for cancer, uraemia, pneumonia and homebound lifestyle, increasing the weighting for cerebrovascular episode and introducing a weighting for age > 70 and for severe dementia.
- *Cohn et al*. consider the PAM index a better predictor of death than of survival, and that CPR can be withheld if the PAM index is > 8 .

CAN THE OUTCOME BE PREDICTED?

- The PAM index contains many of the complications that may arise in a late stage of cancer, and can say something about the extent of the disease.

- Discontinuation of tumour-directed therapy will normally indicate advanced disease.

- A poor physical performance status tells a great deal about the patient's remaining strength to tolerate new stresses.

- Anticipated cardiac arrest is normally part of the terminal stage.

TAKE HOME MESSAGES

- Despite advances, cancer patients still have lower ROSC rate and survival to discharge than patients without cancer.
- Survival of patients with highly treatable/non advanced cancer could be as high as in individuals without cancer.
- Less aggressive use of post-resuscitation procedures in cancer patient, such as TTM, PCI and mechanical support could have a role.
- Multidisciplinary and earlier discussion on DNAR status.