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Impact of cardiopulmonary resuscitation on organ donation in Switzerland

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Summary

AIMS OF THE STUDY: The lack of suitable donor organs limits the number of solid organ transplants. Patients who underwent cardiopulmonary resuscitation (CPR) after cardiac arrest may represent a sizeable subgroup of deceased organ donors, as they often progress to brain death or have life-sustaining therapy withdrawn. We aimed to quantify deceased organ donation after CPR in Switzerland for the first time by analysing the characteristics of potential and utilised organ donors after CPR.

METHODS: Data on deceased adult and paediatric patients who were reported to and approved by Swisstransplant for organ donation were analysed, including both donation after brain death (DBD) and donation after controlled cardiocirculatory death (cDCD) from 2016 to 2018. We analysed baseline characteristics of potential donors who underwent CPR in the context of their hospitalisation, as compared with donors without prior CPR. Considering the varying characteristics between these two donor groups, we assessed the effect of CPR on different allocation outcomes (donor and organ utilisation, organ yield per utilised donor) using multivariable regression. Additionally, we present selected CPR circumstances and compared different subgroups of CPR donors according to duration of CPR and duration of no-flow time.

RESULTS: Of the 461 deceased potential organ donors included in the analysis, 173 (37.5%) underwent CPR. CPR donors were, on average, younger (median age 53 vs 62, p <0.001), had different causes of death (p <0.001), and were more often of the cDCD type (30.1% vs 18.4%, p = 0.004) as compared with non-CPR donors. Of the 173 CPR donors, 152 (87.9%) could be utilised (minimum one organ transplanted), and in the multivariable analysis, utilisation rate was higher in the CPR donor group than in the non-CPR donor group (odds ratio 3.3, 95% confidence interval 1.1–11.5; p = 0.046). Organ specific utilisation of heart, liver, and kidney, and total organ yield per donor, did not differ significantly between CPR and non-CPR donors.

CONCLUSION: Our study reveals that a substantial proportion of deceased organ donors in Switzerland underwent CPR in context of their hospitalisation. CPR donors are different from non-CPR donors with respect to age, cause of death and donation type. However, when carefully selected according to their haemodynamic condition, CPR donors are comparable to non-CPR donors in terms of donor and organ utilisation, as well as the average organ yield. Thus, all patients who are resuscitated from cardiac arrest but who subsequently progress to death should be evaluated for organ donation. How CPR donors compare with non-CPR donors regarding transplant outcomes should be studied further.

***Keywords**: cardiopulmonary resuscitation, organ donation, organ transplantation*

Introduction

Solid organ transplantation is a success story, providing carefully selected candidates with end-stage organ failure a survival benefit and an improved health-related quality of life [1, 2]. According to the International Report on Organ Donation and Transplantation Activities by the Global Observatory on Donation and Transplantation (GODT), more than 139,000 solid organs were transplanted worldwide in 2017, most frequently kidneys and livers. However, despite the remarkable number of transplanted organs, only 10% of global needs were covered, as highlighted in the GODT Report [2]. In Switzerland, 582 solid organ transplants were performed in 2019 while 2149 patients were on the national transplant waiting list, 46 of whom died in 2019 awaiting a life-saving transplant [3]. Thus, the lack of suitable donor organs limits the number of transplants in Switzerland and across the world, as the demand for suitable organs for transplantations continuously outnumbers the availability of donor organs. The current ongoing worldwide coronavirus pandemic is likely to reinforce this, given the fact that countries such as France and the USA reported a steep decline of over 90% and 50%, respectively, in deceased organ transplants during the first wave of the pandemic [4].

In Switzerland, as in many other countries, numerous efforts have been made to expand the deceased donor pool, including reintroduction of donation after controlled cardiocirculatory death (cDCD), ex-vivo machine perfusion of donor organs, and use of so-called extended criteria donors [5]. The latter are donors with conditions that might be limiting for successful donation and transplantation. Ex-

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tended criteria obviously depend on the type of organ; however, unified criteria are not available in the literature and extended criteria are commonly based on expert opinion.

Cardiopulmonary resuscitation (CPR) usually is not one of the extended criteria currently used in the evaluation of deceased donor organs [6]. However, patients who underwent CPR after cardiac arrest are possibly a substantial subgroup of deceased organ donors, as they often progress to brain death (required for organ donation after brain death) or have their life-sustaining therapy withdrawn (required for controlled cardiocirculatory death). Recently published data have demonstrated non-inferior long-term allograft function for organ donation after CPR [7, 8]. Still, there is reluctance among clinicians to accept these organs for transplantation due to concerns of ischaemia-reperfusion injury at CPR and potential post-CPR organ dysfunction [7]. Information on the circumstances in which CPR took place is often incomplete or missing, complicating clinicians' decisions on organ utilisation from organ donors after CPR.

To the authors' knowledge, the extent of deceased organ donation after CPR in Switzerland has not thoroughly been studied to date. Thus, we investigated for the first time the number and characteristics of potential organ donors after CPR, as compared with organ donors without prior CPR. Additionally, we describe the circumstances in which CPR took place and compare different subgroups of CPR donors according to the duration of CPR and the duration of no-flow time.

Materials and methods

Donor data and study populations

Data on potential solid organ donors from the national database "Swiss Organ Allocation System" (SOAS) was retrospectively analysed. SOAS data are mandatorily reported by trained hospital professionals dedicated to organ donation, using standardised online forms, and under supervision of Swisstransplant. We included all Swiss deceased organ donors from 1 January 2016 to 31 December 2018 if they were approved for organ donation by the medical advisors of Swisstransplant, with a minimum of one organ offered for transplantation (n = 463). Included were adult and paediatric donors after brain death (DBD), and after controlled cardiocirculatory death (cDCD), respectively. "Controlled" here means that the ultimately death-causing cardiac arrest was planned in hospital, following the withdrawal of life-sustaining therapy [6]. Two donors were excluded from the subsequent analysis because their next of kin had withdrawn consent for donation only after an organ offer was placed.

We compiled standardised SOAS donor baseline characteristics including sex, age, blood group, cause of death, donation type (DBD vs cDCD), year of hospital admission and whether the donor underwent CPR in context of the hospitalisation resulting in deceased organ donation (see table 1).

For *utilised* (i.e., at least one organ transplanted) donors after CPR we compiled additional data on the donors' medical history, laboratory and supplementary diagnostic results, and the circumstances of CPR. For the latter, all medical and paramedical reports available in SOAS were individually checked by the first author of this study. Additional information on circumstances of CPR included setting (in- vs out-of-hospital, lay vs professional rescuer), estimated time of the event necessitating CPR, no-flow time, low-flow time to return of spontaneous circulation (ROSC), extra-corporeal membrane oxygenation (ECMO) usage, and the estimated duration of all above listed procedures. If the time of the event necessitating CPR was not appropriately documented, 1 hour prior to admission to hospital was used as the default estimated time of event [9]. For further analysis, we grouped the utilised donors after CPR regarding documented duration of CPR and no-flow time, respectively. A study population flowchart is displayed in figure 1.

We analysed data routinely and mandatorily reported to Swisstransplant as mandated by the Federal Office of Public Health (FOPH) and by Swiss law. The Swisstransplant mandate includes data analyses for the purpose of quality assurance and for regular evaluation of organ allocation algorithms in the light of the principle of non-discrimination of recipients on the waiting list as required by law (Transplantation Act). Datasets were analysed in pseudo-anonymised form and all involved researchers signed a confidentiality agreement. Research was conducted in accordance with the Helsinki Declaration as revised in 2013.

Statistical analysis

Baseline characteristics of CPR donors as compared with non-CPR donors

Donors were divided into two groups, donors after CPR in context of their hospitalisation, and donors without prior CPR in context of their hospitalisation. Between these two groups, baseline donor characteristics were compared for quantitative variables by using the t-test or, if the normality assumption was not met, by the non-parametric Wilcoxon rank-sum test. For qualitative variables, Pearson's chi-square test was used, or Fisher's exact test in the case of a small sample size.

Effect of CPR on allocation outcomes (multivariable analysis)

Further, we analysed the effect of CPR (as independent variable) on the three allocation outcomes (dependent variables):

1. donor utilisation (at least one organ transplanted),
2. individual utilisation (organ transplanted) of the heart, the liver, and the kidney, respectively,
3. total organ yield per donor (with the heart, the liver, the lung, two kidneys, the pancreas, and the small bowel, a maximum of seven organs can be transplanted),

using logistic regression for (1) and (2), and linear regression for (3), and adjusting for all baseline donor characteristics presented in table 1, year of hospital admission and blood group (independent variables). The effect of CPR on donor utilisation was analysed in the entire study population (n = 461), the effect of CPR on utilisation of individual organs and on organ yield was analysed in the utilised donor population only (n = 399).

CPR duration and duration of no-flow time

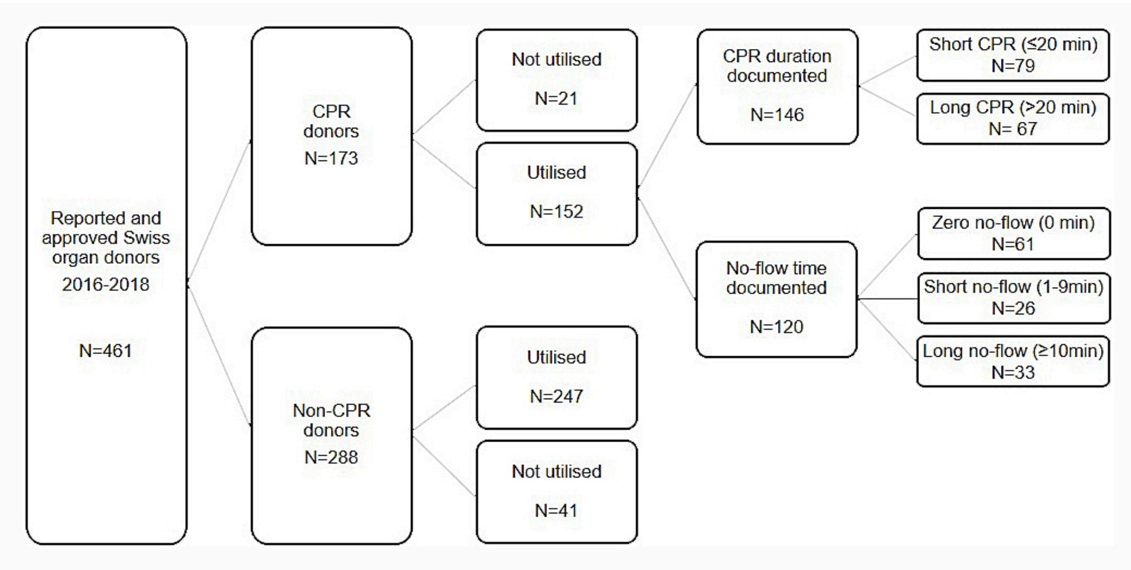
We divided the utilised CPR donors with documented total CPR time (n = 146) into two groups according to CPR duration (≤20 min vs >20 min). These two groups were compared for quantitative variables by using the t-test or, if the normality assumption was not met, by the non-paramet-

Table 1: Baseline characteristics and allocation outcomes of donors who underwent cardiopulmonary resuscitation (CPR) in context of their hospitalisation (CPR donors) as compared with donors without prior CPR in context of their hospitalisation (non-CPR donors).

	Study population n (%)	Non-CPR donors n (%)	CPR donors n (%)	p-value
Total	461 (100)	288 (62.5)	173 (37.5)	
2018	175 (100)	107 (61.1)	68 (38.9)	0.860
2017	164 (100)	105 (64.0)	59 (36.0)	
2016	122 (100)	76 (62.3)	46 (37.7)	
Donor characteristics				
Gender (male)	268 (58.1)	161 (55.9)	107 (61.8)	0.210
Age, median (IQR)	58 (47–70)	62 (50–73)	53 (42–64)	<0.001
Cause of death				<0.001
– CHE	183 (39.7)	130 (52.6)	30 (19.7)	
– ANX	122 (26.5)	6 (2.4)	99 (65.1)	
– CTR	111 (24.1)	83 (33.6)	20 (13.2)	
– CDI/OTH	35 (7.6)	32 (11.1)	3 (1.7)	
– na	10 (2.2)	5 (1.7)	5 (2.9)	
Donation type				0.004
– DBD	356 (77.2)	235 (81.6)	121 (69.9)	
– cDCD	105 (22.8)	53 (18.4)	52 (30.1)	
Allocation outcomes				
Number of utilised donors (at least one organ transplanted)	399 (86.6)	247 (85.8)	152 (87.9)	0.523
Total for subsequent allocation outcomes	399 (100)	247 (61.9)	152 (38.1)	
Heart transplanted, DBD	121 (38.2)	83 (40.3)	38 (34.2)	0.290
Liver transplanted, total	323 (81.0)	196 (79.4)	127 (83.6)	0.299
– DBD	272 (85.8)	173 (84.0)	99 (89.2)	0.205
– cDCD	51 (62.2)	23 (56.1)	28 (68.3)	0.254
Kidney transplanted, total	334 (83.7)	209 (84.6)	125 (82.2)	0.532
– DBD	274 (86.4)	178 (86.4)	96 (86.5)	0.984
– cDCD	60 (73.2)	31 (75.6)	29 (70.7)	0.618
Number of organs transplanted per donor, mean (SD), total	3.1 (±1.5)	3.2 (±1.5)	3.0 (±1.4)	0.332
– DBD	3.4 (±1.5)	3.4 (±1.5)	3.4 (±1.4)	0.834
– cDCD	2.2 (±1.0)	2.2 (±0.9)	2.1 (±1.0)	0.846

ANX = anoxia; cDCD = controlled donation after cardiocirculatory death; CDI = cerebral disease; CHE = cerebral haemorrhage; CTR = cerebral trauma; DBD = donation after brain death; IQR = interquartile range; OTH = other cause of death; na = cDCD donor not deceased within 120 minutes after therapy withdrawal; SD = standard deviation The maximum possible number or organs transplanted per donor (organ yield) here is seven (i.e., heart, lung, liver, 2 kidneys, pancreas and small bowel).

Figure 1: Study population flowchart. CPR = cardiopulmonary resuscitation.



ric Wilcoxon rank-sum test. For qualitative variables, Pearson's chi-square test was used, or Fisher's exact test in the case of a small sample size.

We divided the utilised CPR donors with documented no-flow time (n = 120) into three groups according to no-flow duration: zero (immediate start of CPR, zero minutes of no-flow), short (1–9 min of no-flow) and long no-flow (≥10 min of no-flow). These three groups were compared for quantitative variables by using one-way analysis of variance or, if the normality assumption was not met, by using non-parametric Kruskal-Wallis test. For qualitative variables, Pearson's chi-square test was used, or Fisher's exact test in the case of a small sample size.

We were interested if the aforementioned CPR duration and no-flow time groups differed with regard to baseline donor characteristics, circumstances of CPR (ex- vs in-hospital, professional vs lay rescuer, ECMO usage, duration between CPR and organ explantation), pre-transplant diagnostics, allocation outcomes (individual utilisation of the heart, the liver, and the kidney, and total organ yield per donor). See table 2 and table S1 in the appendix.

For all statistical analyses the freely available software R (version 3.6.1) was used [10].

Results

Of the 461 deceased potential organ donors included in the analysis, 173 donors (37.5%) had undergone CPR in context of their hospitalisation, with no significant trend over the 3-year study period from 2016 to 2018. On average, CPR donors were younger than non-CPR donors (median age 53 vs 62, p <0.001), had different causes of death (p <0.001) and were more often of the cDCD type (30.1% vs 18.4%, p = 0.004). Anoxia was the most frequent cause of death among CPR donors (65.1%), whereas only 2.4% of non-CPR donors died because of anoxia. On the other hand, among non-CPR donors, cerebral haemorrhage (52.6%) and cerebral trauma (33.6%) were the most frequent death causes, whereas only 13.2% and 19.7% of CPR donors, respectively, died of these causes (table 1).

Table 2: Baseline characteristics and selected circumstances of cardiopulmonary resuscitation (CPR) of utilised donors for whom data on duration of no-flow time and CPR were available.

	Duration of no flow time					**Duration of CPR**			
	Study population n (%)	**Zero n (%)**	**Short n (%)**	**Long n (%)**	**p-value**	**Study population n (%)**	**Short n (%)**	**Long n (%)**	**p-value**
Total	120 (100)	61 (50.8)	26 (21.7)	33 (27.5)		146 (100)	79 (54.1)	67 (45.9)	
Mean (SD) duration of total no-flow time, minutes	5.0 (7.7)	0.0 (0.0)	4.7 (1.6)	14.6 (8.6)	<0.001	5.1 (±7.7)	4.33 (±5.4)	5.88 (±9.5)	0.927
Median (IQR) or mean (±SD) duration of CPR time, minutes	20 (15−35)	20 (10−40)	22 (13−25)	20 (15−30)	0.995	25.4 (±17.9)	13.0 (±5.6)	40.6 (±16.2)	<0.001
Donor characteristics									
Gender (male)	72 (60.0)	32 (52.5)	16 (61.5)	24 (72.7)	0.157	88 (60.3)	45 (57.0)	43 (64.2)	0.375
Age, median (IQR)	52 (39−62)	52 (37−64)	50.5 (41−60)	55 (43−59)	0.712	52 (39−62)	57 (43−68)	49 (38−57)	0.008
Cause of death					0.105				<0.001
– CHE	25 (20.8)	16 (26.2)	7 (26.9)	2 (6.1)		30 (20.5)	23 (29.1)	7 (10.4)	
– ANX	79 (65.8)	36 (59.0)	15 (57.7)	28 (84.8)		95 (65.1)	40 (50.6)	55 (82.1)	
– CTR	15 (12.5)	8 (13.1)	4 (15.4)	3 (9.1)		18 (12.3)	13 (16.5)	5 (7.5)	
– CDI/OTH	1 (0.8)	1 (1.6)	0 (0.0)	0 (0.0)		3 (2.1)	3 (3.8)	0 (0.0)	
Donation type					0.963				0.006
– DBD	87 (72.5)	45 (73.8)	19 (73.1)	23 (69.7)		106 (72.6)	50 (63.3)	56 (83.6)	
– cDCD	33 (27.5)	16 (26.2)	7 (26.9)	10 (30.3)		40 (27.4)	29 (36.7)	11 (16.4)	
Circumstances of resuscitation									
CPR ex-hospital	103 (85.8)	46 (75.4)	25 (96.2)	32 (97.0)	0.004	128 (87.7)	70 (88.6)	58 (86.6)	0.709
CPR in-hospital	28 (23.3)	20 (32.8)	3 (11.5)	5 (15.2)	0.053	31 (21.2)	10 (12.7)	21 (31.3)	0.006
CPR by professional	113 (95.0)	55 (91.7)	26 (100)	32 (97.0)	0.350	139 (95.9)	72 (92.3)	67 (100.0)	0.031
CPR time by professional, % of total CPR time, mean (SD)	80% (±27%)	75% (±30%)	83% (±24%)	86% (±23%)	0.254	80% (±27%)	81% (±30%)	79% (±23%)	0.113
CPR by non-professional	53 (44.5)	30 (50.0)	12 (46.2)	11 (33.3)	0.297	62 (43.1)	26 (33.3)	36 (54.5)	0.010
CPR time by non-professional, % of total CPR time, mean (SD)	20% (±27%)	25% (±30%)	17% (±24%)	14% (±23%)	0.179	20% (±27%)	19 (±31%)	21 (±23%)	0.105
ECMO, performed	13 (10.8)	8 (13.1)	2 (7.7)	3 (9.1)	0.796	14 (9.6)	2 (2.5)	12 (17.9)	0.003
Time on ECMO (d), mean (SD), n = 12 (no-flow subgroup), n = 11 (CPR subgroup)	2.5 (±1.8)	2.6 (±1.9)	1.6 (±0.5)	4.0 (n = 1)	0.239	2.4 (±1.7)	4.0 (n = 1)	2.3 (±1.7)	NA
Median event-to-clamp time (h) for organ explantation (IQR)	59 (38−122)	50 (36−112)	45 (35−112)	86 (46−126)	0.074	65 (38 −119)	71 (41−125)	59 (38−97)	0.292

ANX = anoxia; cDCD = controlled donation after cardiocirculatory death; CDI = cerebral disease; CHE = cerebral haemorrhage; CTR = cerebral trauma; DBD = donation after brain death; ECMO = extra-corporeal membrane oxygenation; IQR = interquartile range; NA = group number too small for statistical test; OTH = other cause of death; SD = standard deviation Categories of no-flow time duration: zero (0 min no-flow time, immediate CPR by bystanders), short (1–9 min no-flow time), and long (≥10 min no-flow time). Categories of CPR duration: short (≤20 min of documented CPR) and long (>20 min of documented CPR).

Effect of CPR on donor utilisation and transplantation of heart, liver, and kidney

Of the 173 CPR donors, 152 (87.9%) were utilised (i.e., from those donors at least one organ was eventually transplanted) and of the 288 non-CPR donors, 247 (85.8%) could be utilised (table 1). Thus, CPR donors were more frequently utilised than non-CPR donors, although not significantly. A significantly higher utilisation rate among CPR donors was found in the multivariable analysis adjusting for possibly confounding patient characteristics, the donation type and year of hospital admission: CPR donors were more likely to be utilised, having a minimum of one organ transplanted (odds ratio 3.3, 95% confidence interval 1.1–11.5; p = 0.046; fig. 2a). Of the 152 utilised CPR donors, 38 hearts (34.2%), 127 livers (83.6%) and 125 kidneys (82.2%) could eventually be transplanted. These transplant rates are comparable with the transplant rates of the non-CPR donor group (table 1). The multivariable analysis also showed no significant difference with respect to the transplant rates of heart, liver, or kidney between CPR and non-CPR donors (fig. 2b–d).

Effect of CPR on organ yield

For the 399 utilised donors (i.e. from those donors at least one organ was eventually transplanted), the average organ yield was almost identical for CPR and non-CPR donors, with 3.4 ± 1.4 vs 3.4 ± 1.5 (mean ± standard deviation) organs transplanted per DBD, and 2.1 ± 1.0 vs 2.2 ± 0.9 organs transplanted per cDCD (table 1). Also, in the multivariable analysis adjusting again for possibly confounding patient characteristics, the donation type and year of hospital admission, no significant difference was detected regarding organ yield between CPR and non-CPR donors (fig. 2e).

Duration of no-flow time

As shown in table 2, there were 120 utilised CPR donors with a documented no-flow time. According to our definitions described in the "Material and methods" section, 61 had zero no-flow time (immediate start of CPR, zero minutes of no-flow time), 26 had a short no-flow time (mean duration of no-flow time 4.7 ± 1.6 min), and 33 had a long no-flow time (mean duration of no-flow time 14.6 ± 8.6 min).

Donor characteristics were not significantly different between these three no-flow categories. More short and long no-flow donors were resuscitated ex-hospital as compared with those donors without any no-flow time (96.2% and 97.0% vs 75.4%, p= 0.004). The median "event-to-clamp time for organ explantation", thus the potential recovery time from CPR treatment until start of organ explantation, was the longest for long no-flow donors (86 h), although the difference from short (45 h) and zero (50 h) no-flow donors was non-significant.

Additionally, among long no-flow donors there were significantly more heavy smokers (as measured in pack years). No significant differences were detected with respect to organ diagnostics, blood laboratory results or allocation outcomes between the three no-flow categories (data in table S1 in the appendix).

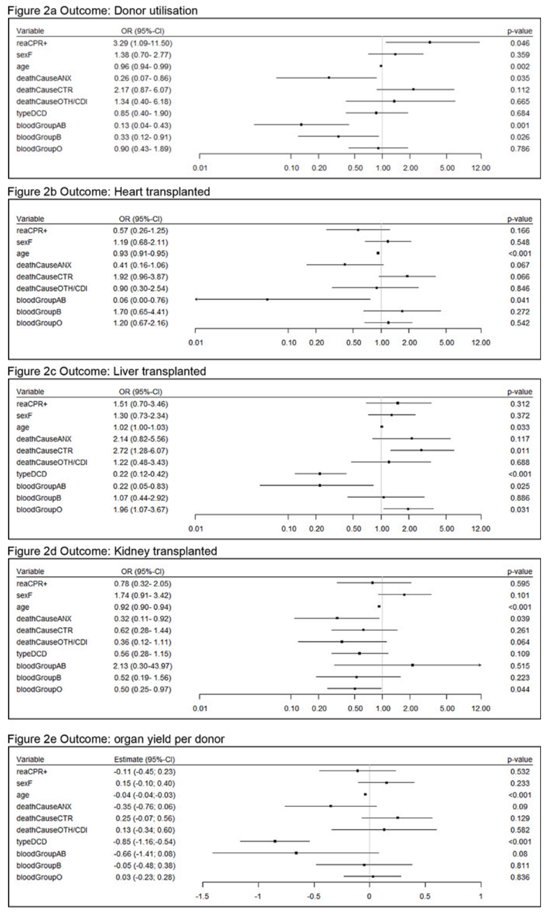
Duration of CPR

As shown in table 2, there were 146 utilised CPR donors with a documented CPR time. According to our definitions described in the "Material and methods" section, 79 had a short CPR (mean duration 13.0 ± 5.95 min) and 67 had a long CPR (mean duration 40.6 ± 16.2 min).

Long CPR donors were younger (median age 49 vs 57, p = 0.008) and included fewer cDCDs (16.4% vs 36.7%, p = 0.006) as compared with short CPR donors. The two groups also differed in their causes of death (p <0.001). Long CPR donors died less frequently of cerebral haemorrhage (10.4% vs 29.1%) and cerebral trauma (7.5% vs 16.5%) when compared with short CPR donors. On the other hand, long CPR donors died more frequently of anoxia (82.1% vs 50.6%).

Long CPR donors were reanimated more often in hospital (31.3% vs 12.7%, p =0.031) and, at least partly, by professionals (100% vs 92.3%, p = 0.031) when compared with short CPR donors. Additionally, long CPR donors were

Figure 2a-e: Odds ratios (a-d), and estimates (e), with 95% confidence intervals of five multivariable regression analyses. Logistic regression of the outcome donor utilisation (a), heart (b), liver (c), and kidneys transplanted (d). Linear regression of the total number of transplanted organs per donor (e). For the variables cause of death and blood group, odds ratios and estimates to the reference cerebral haemorrhage (CHE), and blood group A are given. In the case of the continuous variable age, odds ratios and the estimate correspond to an increase of 1 year. Of note: the variable year of admission/death was included in all regression models but, for reasons of space, is not displayed. ANX = anoxia; CDI = cerebral disease; CPR = cardiopulmonary resuscitation; CTR = cerebral trauma; DCD = donation after cardiocirculatory death; OTH = other.



more frequently on ECMO support at any time point leading to organ procurement (p = 0.003) as compared with short CPR donors.

With regard to laboratory values, liver function tests were more elevated in long CPR donors (data in table S1) when compared with short CPR donors; however, the analysis of laboratory values has to be interpreted cautiously because individual serial data were not available in our dataset.

Discussion

In our retrospective database study, we investigated for the first time the extent of solid organ donation from donors after CPR in Switzerland. During the 3-year study period from 2016 to 2018, 37.5% of deceased hospitalised patients reported to and approved by Swisstransplant for organ donation had undergone CPR. To the best of our knowledge, there are in the literature no similar studies for comparison that systematically investigated the extent of organ donation after CPR on a national level. A recent single-centre study from Pittsburgh, which analysed 12,130 deaths, found that 34% of 435 utilised donors were CPR donors [7]. This proportion compares very well with the 152 (38%) CPR donors of 399 utilised donors we found in our study. At the Pittsburgh centre, potential organ donors after CPR and their relatives were more likely to consent to organ donation as compared with potential non-CPR donors [7]. We do not know if the latter is also true for our study population since we included only donors who had already consented to donation.

In our study population, CPR donors were, on average, significantly younger, with a median age of 53 years, as compared with 62 years in non-CPR donors. The age difference was particularly pronounced in the age group of 65+; less than a quarter of CPR donors belonged to this age group compared with over 40% among non-CPR donors (data not shown). Other studies recently found similar results [11–13]. Anoxia was the cause of death in 122 (26.5%) patients in our study, which is comparable to recent data published elsewhere [14]. However, anoxia was – not unexpectedly in the context of post-CPR – more frequent among CPR donors than among non-CPR donors (65.1% vs 2.4%, p <0.001), which is comparable to the findings of Mehdiani et al. published in 2020. They suggested that the overrepresentation of anoxia as cause of death in their CPR donor group might be explained by the fact that these donors more often committed suicide by strangulation, and that this suicide form, in turn, might be related to male gender and younger donor age [13]. In our CPR donor group, suicide by strangulation was documented for at least 16 of 173 (9%) donors (data not shown). Therefore, this form of death, the young age and male gender in our CPR donor group might be related. Furthermore, cDCD was significantly more frequent in our CPR donor group as compared with our non-CPR group. These findings are also consistent with the previously cited single-centre study from Pittsburgh [7].

In our study, utilisation (at least one organ transplanted) of CPR and non-CPR potential donors was comparable, at over 85% in both groups. After adjusting for possible confounding patient factors (sex, age, cause of death, blood group, donation type, year of hospitalisation), CPR donors were even more likely to be utilised. However, with this result it is important to recall that we analysed preselected potential donors (reported to, and approved by, Swisstransplant for organ donation, respectively). Focussing on a larger data set but looking only at DBD, Sandroni and colleagues conducted a systematic review and meta-analysis investigating prevalence of brain death in adults after CPR and the rate of organ donation among brain dead patients, including 26 studies with a total of 23,388 patients [15]. The authors reported an overall organ donation rate of 41.8% (20.2−51.0%) among brain dead patients after CPR. We found in our study that over 30% of CPR donors were not brain dead but controlled cardiocirculatory deaths (planned cardiac arrest following the withdrawal of life-sustaining therapy). Thus, in the evaluation of the potential for organ donation in CPR patients, not only DBD but also cDCD should be considered if, of course, a cDCD programme is available at all.

In our study population, organ yield was almost identical for CPR and non-CPR utilised donors, with an average of 3.4 organs transplanted per DBD, and just over two organs transplanted per cDCD. This result remained unchanged in the multivariable analysis. Further, the multivariable analysis showed no significant difference for the transplant rate of the heart, the liver or the kidneys between CPR and non-CPR donors. These findings are comparable to international findings [8, 11, 13, 14] and we thus believe that they may be relevant for other countries, in particular for those who have established cDCD programmes. To achieve a high rate of organ utilisation as we found in our potential CPR donor group, we further believe that clinical interventions aiming for best practice donor management in the intensive care unit, including steroid application, desmopressin and diuretic use, are key factors, as Selck et al revealed in their large US database analysis [16]. We also think that with CPR donors it is crucial to have a well-functioning rescue chain that includes everyone from the lay rescuer, the paramedical team and the emergency department to the clinician on the intensive care unit, as Cohen et al. discussed in their analysis of organ donor utilisation [14]. In Switzerland, donor management consensus guidelines are implemented to achieve best clinical practice in donor detection and management by Swisstransplant and the “Comité National du Don d’Organes”.

Looking at heart transplantations from CPR donors, German colleagues Mehdiani et al. found an interval between CPR and organ explantation of 112 ± 74 hours (mean ± standard deviation). They also found that the absolute organ recovery time per se had no impact on short and mid-term recipient survival [13]. However, a longer interval between CPR and organ explantation of course means more time for the organs to recover from the CPR procedure, which would be most important for donors who had prolonged durations of CPR and/or no-flow times. The median interval time between CPR and organ explantation of our CPR donors was almost 2 days less than in the aforementioned study, 59 hours (interquartile range 38−122) and 65 hours (38−119) “event-to-clamp time for organ explantation” (table 2). There are several possible explanations for this substantial difference. First, in our CPR donor group not only the heart but all transplantable organs were included. Second, one third of our CPR donors were cD-

CDs where, after the planned cardiac arrest for organ donation, the warm ischaemia time should be as short as possible to prevent further damage to the organs. In the study of Mehdiani et al. no cDCD was included. However, the relatively short organ recovery time we found in our Swiss CPR donors possibly can also be explained by the legally binding timeframes that apply for organ donation in Switzerland. After therapy withdrawal, brain death diagnostics must be completed within 48 hours, and after death is determined, organ-preserving preparatory medical measures may be performed only for a maximum of 72 hours [17]. The latter implicates that organ allocation and procurement must be completed within 72 hours after death determination.

In Switzerland, potential organ donors after CPR are evaluated based on their haemodynamic condition and the estimated time the organs need to recover from the CPR intervention. Apart from that, the criteria for organ acceptance are the same for CPR and non-CPR donors. Sometimes the given organ recovery time is too short for hemodynamic instable patients after CPR with multiorgan failure to be considered as organ donors. With these patients, it would be crucial to delay the start of organ explantation until a sufficiently long hemodynamic stable period is achieved. Of course, a delayed start of organ explantation must be within the legally binding timeframes. Also, such a decision must be taken together with intensive care physicians, carefully considering the available intensive care resources, and with the next of kin who need to feel comfortable with such a procedure.

Our study shows that with careful evaluation, considering the hemodynamic condition, and with optimal donor management, many CPR patients can be included in deceased organ donation. As long as sufficient time for a hemodynamic stabilisation between CPR intervention and start of organ explantation can be given, average organ utilisation and total organ yield per CPR donor is comparable to non-CPR donors. Therefore, all patients who are resuscitated from cardiac arrest but subsequently progress to brain death or controlled cardiocirculatory death should be evaluated for organ donation. This is now also the official recommendation of the American Heart Association, as published very recently in their 2020 Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care [18].

Whether CPR donors can also be suggested in terms of transplantation outcomes is outside of the scope of this study. There is an ongoing discussion among clinicians in the field of solid organ transplantation regarding the viability of organs from deceased donors after CPR and their post-transplant graft function. In 2016, a systematic review compared the viability and post-transplant outcomes from almost 15,000 transplantations from CPR vs non-CPR donors [8]. In this review, no difference in early, 1-year, and 5-year post-transplant graft function was found. The effect of the cardiac arrest on procured organs seemed to be reversible. Only in uncontrolled DCDs after CPR, delayed allograft function occurred early post-transplant, likely due to lack of return of spontaneous circulation by CPR; however, graft function of uncontrolled DCDs after CPR at 1- and 5-years post-transplant was again similar to that of non-CPR donors [8]. A recent study analysing donor data from 2010–2018 in the United States compared up to 10-year recipient and graft survival in simultaneous pancreas and kidney transplantation and found no difference in patient and graft survival between CPR and non-CPR donor organs [19]. Also and most recently, Mehdiani et al., who investigated up to 1-year survival of their heart transplant patients, found no significant difference in short and mid-term outcomes between CPR and non-CPR donors [13].

Strength and limitations

It is the strength of our study to present for the first-time numbers and characteristics of deceased organ donors after CPR on a national level, with an analysis of a large and representative donor population, including cDCD. For the analysis of CPR vs non-CPR donors, we used multivariable regression, which allowed us to adjust for possibly confounding patient factors. Further, we were able to include and investigate many CPR-related circumstances, which usually are not readily available in deceased patient databases.

However, our study also has limitations. Only preselected CPR patients who had been identified and reported as potential organ donors, and had been approved for donation by Swisstransplant, were analysed. In particular, the number of CPR patients in general was not available to us, which is why we probably underestimate the true potential of CPR patients for deceased organ donation. Information on CPR circumstances was not available for 6 (CPR duration), and for 32 (no-flow time) of 152 utilised CPR donors, creating possible bias in this subanalysis. Additionally, for the analysis of CPR duration and no-flow time we used a univariable approach, which does not account for possible confounders. Post-transplant outcome data were either not available to us or of very poor quality. Based on the analysis of our data we therefore are not able to contribute to the discussion of how CPR donors compare with non-CPR donors with regard to graft and recipient survival.

Conclusion

Organ donation after CPR is underreported in the literature. For the first time, we show that over a third of Swiss deceased potential organ donors underwent CPR. When CPR donors are carefully selected and managed according to their haemodynamic condition, donor and organ utilisation as well as total organ yield per donor is comparable to non-CPR donors. Thus, all patients who are resuscitated from cardiac arrest but who subsequently progress to death should be evaluated for organ donation. How CPR donors compare with non-CPR donors regarding transplant outcomes should be studied further.

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Appendix

Supplementary table

Notes

Between these groups (short/long CPR time, ≤20 min/ >20 min), baseline donor characteristics etc., allocations were compared for quantitative variables by using the t-test or, if the normality assumption was not met, by non-parametric Wilcoxon rank-sum test. For qualitative variables, Pearson's chi-square test was used, or Fisher's exact test when the sample size was small (i.e,. all with <5/group).

Between these groups (zero/short/long no-flow time, 0/ 1–9/≥10 min), baseline donor characteristics, allocation were compared for quantitative variables by using one-way ANOVA or, if the normality assumption was not met, by non-parametric Kruskal-Wallis test. For qualitative variables, Pearson's chi-square test was used, or Fisher's exact test when the sample size was small (i.e., all with <5/ group).

Explanation for laboratory values: The number in parenthesis behind blood lab results indicates the interval of hours the blood sample was taken after the CPR treatment of each donor. The "last value", is a representation of the individual's last available value before organ procurement took place in each donor, independent of when after CPR the blood sample was taken.

Because of the retrospective nature of this study, the number of lab values in each time interval is very heterogeneous (noted with n's). Also, no conclusions towards longitudinal individual lab value development can be drawn from these results. Which is why we included the value "transition", representing the percentage of recovery of the lab value in each individual donor from their last value before organ procurement to the highest individual registered value after CPR.

Table S1: Complete table for the analysis of the effect of CPR duration and no-flow time; included are only utilised donors (at least one organ transplanted) for whom either the duration of no-flow time, or the duration of CPR was documented.

Characteristics		No flow study population n (%)	Zero no flow n (%)	Short no flow n (%)	Long no flow n (%)	p-value	CPR duration study population n (%)	Short CPR n (%)	Long CPR n (%)	p-value
Total		120 (100)	61 (50.8)	26 (21.7)	33 (27.5)		146 (100)	79 (54.1)	67 (45.9)	
Year of admission/ death	2018	46 (100)	25 (54.3)	8 (17.4)	13 (28.3)	0.843	57 (100)	33 (57.9)	24 (42.1)	0.644
	2017	39 (100)	18 (46.2)	9 (23.1)	12 (30.8)		51 (100)	25 (49.0)	26 (51.0)	
	2016	35 (100)	18 (51.4)	9 (25.7)	8 (22.9)		38 (100)	21 (55.3)	17 (44.7)	
Patient factors										
Gender	Male	72 (60.0)	32 (52.5)	16 (61.5)	24 (72.7)	0.157	88 (60.3)	45 (57.0)	43 (64.2)	0.375
	Female	48 (40.0)	29 (47.5)	10 (38.5)	9 (27.3)		58 (39.7)	34 (43.0)	24 (35.8)	
Age	Years, median (IQR)	52 (39−62)	52 (37−64)	50.5 (41−60)	55 (43−59)	0.712	52 (39−62)	57 (43−68)	49 (38−57)	0.008
Cause of death	CHE	25 (20.8)	16 (26.2)	7 (26.9)	2 (6.1)	0.105	30 (20.5)	23 (29.1)	7 (10.4)	<0.001
	ANX	79 (65.8)	36 (59.0)	15 (57.7)	28 (84.8)		95 (65.1)	40 (50.6)	55 (82.1)	
	CTR	15 (12.5)	8 (13.1)	4 (15.4)	3 (9.1)		18 (12.3)	13 (16.5)	5 (7.5)	
	CDI/OTH	1 (8.0)	1 (1.6)	0 (0.0)	0 (0.0)		3 (2.1)	3 (3.8)	0 (0.0)	
Donation type	DBD	87 (72.5)	45 (73.8)	19 (73.1)	23 (69.7)	0.963	106 (72.6)	50 (63.3)	56 (83.6)	0.006
	DCD	33 (27.5)	16 (26.2)	7 (26.9)	10 (30.3)		40 (27.4)	29 (36.7)	11 (16.4)	
Blood group	A	65 (54.2)	34 (55.7)	14 (53.8)	17 (51.5)	0.166	75 (51.4)	39 (49.4)	36 (53.7)	945
	O	44 (36.7)	21 (34.4)	7 (26.9)	16 (48.5)		53 (36.6)	30 (38.0)	23 (34.3)	
	B	9 (7.5)	5 (8.2)	4 (15.4)	0 (0.0)		14 (9.6)	8 (10.1)	6 (9.0)	
	AB	2 (1.7)	1 (1.6)	1 (3.8)	0 (0.0)		4 (2.7)	2 (2.5)	2 (3.0)	
BMI	kg/m^2, median (IQR)	25.7 (22.9−27.8)	25.7 (23.1−28.7)	25.9 (22.8−27.7)	24.7 (22.5−27.5)	0.577	25.7 (22.9−28.3)	25.1 (22.8−28.0)	26.3 (23.2−28.4)	0.389
Circumstances of resuscitation										
Total CPR time	Minutes, mean (SD)						25.4 (±17.9)	13.0 (±5.95)	40 (±16.2)	<0.001
No-flow-time	Minutes, mean (SD)						5.1 (±7.7)	4.33 (±5.37)	5.88 (±9.51)	0.927
	0 minutes (zero)						60 (50.4)	31 (50.8)	29 (50.0)	0.989
	1–9 minutes (short)						26 (21.8)	13 (21.3)	13 (22.4)	
	≥10 minutes (long)						33 (27.7)	17 (27.9)	16 (27.6)	
	Unknown						27	18	9	
No-flow time	Min, mean (SD)	5.0 (7.7)	0.0 (0.0)	4.7 (1.6)	14.6 (8.6)	<0.001				
CPR time	Min, median (IQR)	20 (15−35)	20 (10−40)	22 (13−25)	20 (15−30)	0.995				
	≤20 minutes (short)	61 (51.3)	31 (51.7)	13 (50.0)	17 (51.5)	0.989				
	>20 minutes (long)	58 (48.7)	29 (48.3)	13 (50.0)	16 (48.5)					
	Unknown	1	1							
CPR by professional	Yes	113 (95.0)	55 (91.7)	26 (100)	32 (97.0)	0.350	139 (95.9)	72 (92.3)	67 (100.0)	0.031
CPR time by professional	Minutes, mean (SD)	20.8 (±17.1)	19.4 (±15.8)	21.0 (±16.9)	23.5 (±19.7)	0.543	20.3 (±16.3)	10.4 (±6.1)	31.9 (±16.9)	<0.001
	As percentage of total CPR time, mean (SD)	80% (±27%)	75% (±30%)	83% (±24%)	86% (±23%)	0.254	80% (±27%)	81% (±30%)	79% (±23%)	0.113
	Unknown	1					1	1	0	
CPR by non-professional	Yes	53 (44.5)	30 (50.0)	12 (46.2)	11 (33.3)	0.297	62 (43.1)	26 (33.3)	36 (54.5)	0.010
CPR time by non-professional	Minutes, mean (SD)	5.2 (±8.0)	6.4 (±8.1)	5.6 (±10.4)	2.8 (±4.5)	0.129	5.0 (±7.7)	2.5 (±4.2)	8.0 (±9.6)	<0.001
	As percentage of total CPR time, mean (SD)	20% (±27%)	25% (±30%)	17% (±24%)	14% (±23%)	0.179	20% (±27%)	19 (±31%)	21 (±23%)	0.105
	Unknown	1					2	1	1	
CPR ex-hospital	Yes	103 (85.8)	46 (75.4)	25 (96.2)	32 (97.0)	0.004	128 (87.7)	70 (88.6)	58 (86.6)	0.709
CPR time ex-hospital	Mean (SD)	20.3 (±15.6)	17.7 (±16.8)	23.0 (±14.0)	23.0 (±14.2)	0.073	20.5 (±15.6)	11.7 (±7.0)	30.8 (±16.6)	<0.001
CPR time ex-hospital	As percentage of total	82% (±36%)	72% (±43%)	93% (±25%)	92% (±25%)	0.015	85% (±34%)	88% (±33%)	81% (±36%)	0.044

Table S1: Complete table for the analysis of the effect of CPR duration and no-flow time; included are only utilised donors (at least one organ transplanted) for whom either the duration of no-flow time, or the duration of CPR was documented.

	CPR time, mean (SD)									
CPR in-hospital	Yes	28 (23.3)	20 (32.8)	3 (11.5)	5 (15.2)	0.053	31 (21.2)	10 (12.7)	21 (31.3)	0.006
CPR time in-hospital	Mean (SD)	5.7 (±13.8)	7.8 (±14.9)	3.7 (±13.3)	3.4 (±11.6)	0.054	4.8 (±12.7)	1.2 (±3.9)	9.1 (±17.3)	0.002
	As percentage of total CPR time, mean (SD)	18% (±35%)	28% (±43%)	7% (±24%)	8% (±23%)	0.024	15% (±33%)	11% (±31%)	19% (±36%)	0.014
CPR Event-to-clamp time for organ explantation	Hours, median (IQR)	59 (38−122)	50 (36−112)	45 (35−112)	86 (46−126)	0.074	64.6 (38.3−119.1)	70.7 (40.9−125.0)	58.6 (38.1−96.7)	0.292
	Unknown	0					0			
Medical history										
Heart disease	Yes	35 (29.2)	19 (31.1)	6 (23.1)	10 (30.3)	0.740	46 (31.5)	25 (31.6)	21 (31.3)	0.969
	Unknown	0					0			
Lung disease	Yes	14 (11.7)	7 (11.5)	4 (15.4)	3 (9.1)	0.810	16 (11.0)	7 (8.9)	9 (13.4)	0.378
	Unknown	0					0			
Liver disease	Yes	2 (1.7)	1 (1.6)	0 (0.0)	1 (3.0)	1	5 (3.4)	1 (1.3)	4 (6.0)	0.182
	Unknown	1		1			1	1	0	
Kidney disease	Yes	9 (7.6)	6 (9.8)	0 (0.0)	3 (9.4)	0.300	11 (7.6)	9 (11.5)	2 (3.0)	0.238
	Unknown	1			1		1	1	0	
Hypertension	Yes	48 (40.0)	26 (42.6)	9 (34.6)	13 (39.4)	0.781	55 (37.7)	34 (43.0)	21 (31.3)	0.146
	Unknown	0					0			
Diabetes	Yes	14 (11.7)	6 (9.8)	3 (11.5)	5 (15.2)	0.757	18 (12.3)	9 (11.4)	9 (13.4)	0.709
	Unknown	0					0			
Infectious diseases	Yes	2 (1.7)	2 (3.3)	0 (0.0)	0 (0.0)	0.718	2 (1.4)	1 (1.3)	1 (1.5)	1
	Unknown	0					0			
Cancer	Yes	2 (1.7)	2 (3.3)	0 (0.0)	0 (0.0)	0.718	4 (2.7)	3 (3.8)	1 (1.5)	0.625
	Unknown	0					0			
Smoker (current)	Yes	43 (37.4)	18 (31.6)	11 (42.3)	14 (43.8)	0.440	52 (37.7)	25 (34.7)	27 (40.9)	0.454
	Unknown	5	4		1		8	7	1	
Pack years	Years, mean (SD)	11.3 (±15.2)	9.1 (±15.0)	9.3 (±12.8)	16.8 (±16.5)	0.019	10.6 (±14.7)	11.8 (±16.6)	9.3 (±12.3)	0.891
	Unknown	11	6	2	3		17	11	6	
Alcohol	Yes	54 (45.0)	29 (47.5)	8 (30.8)	17 (51.5)	0.240	61 (42.1)	31 (39.7)	30 (44.8)	0.541
	Unknown	0					1	1	0	
Drugs	Yes	13 (11.0)	3 (4.9)	4 (16.0)	6 (18.8)	0.068	19 (13.2)	10 (12.8)	9 (13.6)	0.885
	Unknown	2		1	1		2	1	1	
Clinical data (after admission)										
ECMO	Performed	13 (10.8)	8 (13.1)	2 (7.7)	3 (9.1)	0.796	14 (9.6)	2 (2.5)	12 (17.9)	0.003
Time on ECMO	Days, mean (SD), n = 12 / n = 11	2.52 (±1.75)	2.6 (±1.9)	1.6 (±0.5)	4.0 (NA)*	0.239	2.44 (±1.70)	4 (N=1)	2.3 (±1.7)	NA
Organ diagnostics										
Echocardiography	Performed	78 (65.5)	42 (70.0)	18 (69.2)	18 (54.5)	0.294	97 (64.8)	46 (59.0)	51 (76.1)	0.028
	Unknown	1	1				1	1	0	
Echocardiography EF in percent	Mean (SD), n = 78 / n = 96	47.6 (±17.1)	44.6 (±19.0)	48.5 (±13.7)	53.3 (±14.6)	0.185	48.9 (±16.5)	51.3 (±14.9)	46.6 (±17.7)	0.213
Echocardiography abnormalities	Yes, n = 77 / n=95	43 (55.8)	24 (57.1)	8 (50.0)	11 (57.9)	0.868	51 (53.7)	27 (58.7)	24 (49.0)	0.343
Echocardiography valve abnormalities	Yes, n = 77 / n = 95	18 (23.4)	12 (28.6)	3 (18.8)	3 (15.8)	0.591	24 (25.3)	12 (26.1)	12 (24.5)	0.858
Coronary angiography	Performed	51 (45.1)	24 (43.6)	13 (52.0)	14 (42.4)	0.732	63 (45.7)	30 (40.0)	33 (52.4)	0.146
	Unknown	7	6	1			8	4	4	
Coronary stenosis	Yes, n = 51 / n = 63	28 (54.9)	13 (54.2)	6 (46.2)	9 (64.3)	0.636	32 (50.8)	14 (46.7)	18 (54.5)	0.532
Liver abnormalities	Yes	18 (15.3)	9 (15.3)	5 (19.2)	4 (12.1)	0.708	21 (14.6)	12 (15.4)	9 (13.6)	0.767
	Unknown	2	2				2	1	1	
Liver steatosis	Yes	15 (12.7)	7 (11.9)	4 (15.4)	4 (12.1)	0.877	19 (13.2)	11 (14.1)	8 (12.1)	0.726
	Unknown	2	2				2	1	1	
Kidney lesions	Yes	33 (27.7)	16 (26.7)	7 (26.9)	10 (30.3)	0.927	39 (26.9)	27 (34.2)	12 (18.2)	0.031
	Unknown	1	1				1	0	1	
Blood laboratory results										
Creatinine (0–12 h)	n	112	56	25	31		131	72	59	
	µmol/l, mean (SD)	113 (±47)	110 (±39)	108 (±28)	124 (±67)	0.511	114 (±46)	111 (±52)	117 (±37)	0.050

Table S1: Complete table for the analysis of the effect of CPR duration and no-flow time; included are only utilised donors (at least one organ transplanted) for whom either the duration of no-flow time, or the duration of CPR was documented.

Creatinine (13–24 h)	n	50	27	12	11		57	21	36	
	µmol/l, mean (SD)	115 (±60)	117(±66)	103 (±27)	125 (±71)	0.780	118 (±60)	104 (±43)	126 (±67)	0.290
Creatinine (25–36 h)	n	36	21	8	7		42	23	19	
	µmol/l, mean (SD)	126 (±100)	121(±94)	109 (±56)	163 (±153)	0.513	122 (±96)	121 (±101)	124 (±93)	0.4713
Creatinine (37–48 h)	n	21	11	5	5		22	9	13	
	µmol/l, mean (SD)	113 (±103)	146(±133)	65 (±35)	87 (±27)	0.348	117 (±106)	68 (±27)	150 (±127)	0.038
Creatinine (last value)	n	120	61	26	33		145	79	66	
	µmol/l, mean (SD)	108 (±79)	114(±89)	95 (±44)	106 (±82)	0.939	107 (±76)	99 (±61)	116 (±91)	0.100
Creatinine transition (last-max/max) including 15 resp. 17 donors with last = max value (0%); excluding 3 resp. 5 donors with only one measurement	n	117	58	26	33		140	75	65	
	Percent, mean (SD)	–17% (±30%)	–15% (±31%)	–19% (±22%)	–19% (±34%)	0.671	–17% (±30%)	–18% (±32%)	–15% (±27%)	0.524
ASAT (0–12 h)	n	105	55	22	28		123	68	55	
	µmol/l, mean (SD)	273 (±312)	241 (±278)	275 (±312)	336 (±371)	0.338	303 (±370)	257 (±392)	360 (±335)	0.001
ASAT (13–24 h)	n	46	25	12	9		53	20	33	
	µmol/l, mean (SD)	328 (±434)	259 (±247)	211 (±153)	678 (±818)	0.238	330 (±418)	169 (±172)	428 (±490)	0.001
ASAT (25–36 h)	n	38	23	8	7		45	25	20	
	µmol/l, mean (SD)	294 (±380)	201 (±182)	314 (±340)	577 (±714)	0.133	283 (±352)	178 (±187)	413 (±459)	0.002872
ASAT (37–48 h)	n	19	9	5	5		21	9	12	
	µmol/l, mean (SD)	180 (±185)	113 (±112)	249 (±281)	231 (±175)	0.198	183 (±764)	81 (±48)	260 (±197)	0.004
ASAT (last value)	n	120	61	26	33		145	79	66	
	µmol/l, mean (SD)	170 (±250)	145 (±142)	152 (±158)	229 (±413)	0.591	165 (±232)	118 (±124)	222 (±308)	<0.001
ASAT transition (last-max/max) Including 10 resp. 16 donors with last = max value (0%); excluding 9 resp. 10 donors with only one measurement	n	111	56	23	32		132	71	61	
	Percent, mean (SD)	–29% (±74%)	–24% (±92%)	–46% (±25%)	–27% (±59%)	0.567	–32% (±69%)	–23% (±89%)	–43% (±31%)	0.237
ALAT (0–12 h)	n	106	57	20	29		124	69	55	
	µmol/l, mean (SD)	183 (±167)	153 (±148)	220 (±150)	219 (±206)	0.056	198 (±184)	153 (±152)	255 (±206)	<0.001
ALAT (13–24 h)	n	47	25	12	10		53	19	34	
	µmol/l, mean (SD)	202 (±237)	142 (±143)	156 (±100)	407 (±400)	0.074	208 (±234)	120 (±136)	257 (±263)	0.005
ALAT (25–36 h)	n	38	23	8	7		45	25	20	
	µmol/l, mean (SD)	190 (±290)	123 (±154)	144 (±99)	459 (±562)	0.012	191 (±268)	132 (±138)	264 (±363)	0.02669
ALAT (37–48 h)	n	19	9	5	5		21	9	12	
	µmol/l, mean (SD)	145 (±151)	115 (±118)	125 (±88)	220 (±238)	0.555	429 (±1261)	100 (±102)	209 (±163)	0.049
ALAT (last value)	n	120	61	26	33		145	79	66	
	µmol/l, mean (SD)	127 (±192)	98 (±98)	106 (±75)	197 (±329)	0.329	132 (±191)	97 (±129)	174 (±239)	<0.001
ALAT transition (last-max/max) including 12 donors with last = max value (0%); excluding 10 donors with only one measurement	n	111	58	21	32		135	74	61	
	Percent, mean (SD)	–28% (±47%)	–25% (±54%)	–44% (±28%)	–23% (±44%)	0.211	–30% (±45%)	–27% (±53%)	–34% (±34%)	0.657
eGFR CKD EPI from latest creatinine	n	120	61	26	33		146	79	67	
	ml/min, mean (SD)	71.0 (±37.3)	69.1 (±34.6)	75.0 (±50.0)	71.2 (±32.8)	0.906	70.6 (±37.1)	74 (±39.9)	66.6 (±33.5)	0.298
Allocation outcomes										
Heart transplanted										

Table S1: Complete table for the analysis of the effect of CPR duration and no-flow time; included are only utilised donors (at least one organ transplanted) for whom either the duration of no-flow time, or the duration of CPR was documented.

	DBD	25 (28.7)	14 (31.1)	5 (26.3)	6 (26.1)	0.879	34 (32.1)	19 (38.0)	15 (26.8)	0.217
Liver transplanted										
	Total	99 (82.5)	49 (80.3)	22 (84.6)	28 (84.8)	0.857	121 (82.9)	65 (82.3)	56 (83.6)	0.835
	DBD	76 (87.4)	37 (82.2)	17 (89.5)	22 (95.7)	0.297	94 (88.7)	45 (90.0)	49 (87.5)	0.685
	DCD	23 (69.7)	12 (75.0)	5 (71.4)	6 (60.0)	0.881	27 (67.5)	20 (69.0)	7 (63.6)	1
Kidney transplanted										
	Total	100 (83.3)	50 (82.0)	24 (92.3)	26 (78.8)	0.362	120 (82.2)	65 (82.3)	55 (82.1)	0.976
	DBD	76 (87.4)	40 (88.9)	18 (94.7)	18 (78.3)	0.267	92 (86.8)	44 (88.0)	48 (85.7)	0.729
	DCD	24 (72.7)	10 (62.5)	6 (85.7)	8 (80.0)	0.535	28 (70.0)	21 (72.4)	7 (63.6)	0.674
Number of organs transplanted per donor							146 (100%)	79 (100%)	67 (100%)	
Total	Mean (SD)	3.0 (±1.3)	3.0 (±1.3)	3.3 (±1.4)	2.8 (±1.3)	0.417	3.0 (±1.4)	3.0 (±1.4)	3.0 (±1.3)	0.992
DBD	Mean (SD)	3.3 (±1.3)	3.3 (±1.3)	3.6 (±1.4)	3.2 (±1.4)	0.601	3.3 (±1.4)	3.5 (±1.4)	3.2 (±1.3)	0.223
DCD	Mean (SD)	2.2 (±1.0)	2.2 (±1.1)	2.6 (±1.0)	2.1 (±0.9)	0.616	2.1 (±1.0)	2.1 (±1.0)	2.1 (±1.1)	0.905

ALAT = alanine aminotransferase; ANX = anoxia; ASAT = aspartate aminotransferase; CDI = cerebral disease; CHE = cerebral haemorrhage; CTR = cerebral trauma; DBD = donation after brain death; DCD = controlled donation after cardiocirculatory death; ECMO = extra-corporeal membrane oxygenation; EF = ejection fraction; eGFR = estimated glomerular filtration rate; IQR = interquartile range; OTH = other cause of death; SD = standard deviation