Irreversible Total Loss of Brain Function and Organ Donation in Patients with Aneurysmal Subarachnoid Hemorrhage

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■ OBJECTIVE: **Aneurysmal subarachnoid hemorrhage (aSAH) is a life-threatening disease with an often fatal clinical course leading to irreversible loss of brain function (ILBF) (i.e., brain death). The purpose of this study was to assess the prevalence and characteristics of patients with aSAH who became organ donors after diagnosis of ILBF.**

■ METHODS: **Anonymized clinical data sets of 395 patients treated for aSAH at a university medical center from January 2011 to December 2016 were retrospectively analyzed. Prevalence of consent for organ donation and clinical characteristics, including parameters for diagnosis of irreversible loss of brain function, were assessed.**

■ RESULTS: **After initial admission to the intensive care unit, 18.0% of patients (n = 71) died (Glasgow Outcome Scale score 1). Intracerebral hemorrhage occurred in 42.3% of patients who died, aneurysmal rebleeding occurred in 19.7%, and intraventricular hemorrhage occurred in 87.3%. In 50.7% of patients who died (n = 36), ILBF was diagnosed, and 32.4% (n = 23) of these patients became organ donors. In 55.6%, additional diagnostic electroencephalography was performed. Male patients significantly more often became organ donors than female patients (P = 0.008). ILBF with subsequent organ donation was predominantly seen in patients <60 years old. A total 85 of organs were explanted for donation, including 42 kidneys, 21 livers, 3 pancreas, 11 hearts and 8 lungs.**

■ CONCLUSIONS: **ILBF in the setting of fatal aSAH is a prevalent diagnosis with complex demands for neurointensive care physicians. We demonstrated the clinical characteristics and epidemiologic factors of patients with aSAH converting to organ donors.**

INTRODUCTION

Aneurysmal subarachnoid hemorrhage (aSAH) is an acute life-threatening disease that is associated with a mortality rate of approximately 25%.[1] In many patients, death results from an irreversible loss of brain function (ILBF) (i.e., brain death), rendering many patients with aSAH eligible for a potential organ donation.[2] As a result of the growing disparity between organ demand and availability, waiting lists are constantly growing, and the ethical demands for physicians working in intensive care units (ICUs) to ensure consistent assessment of potential organ donors are increasing. Together, these factors render organ donation in the setting of neurointensive care management a sensitive topic where deliberate practice guidelines are required.[3]

Although organ donation rates have decreased in Germany over the past 5 years,[4] international rates have remained stable over the past decade.[5] Introducing best practice guidelines for referral of potential organ donors can lead to significant improvement of organ donor conversion rates.[6,7] Various factors, including family communication guidelines,[8] designating a trained physician to handle family interaction,[9,10] and adapting to ethnicity-specific requirements,[11] can contribute to enhance organ donation.

Patients with ILBF after resuscitation from cardiac arrest donated organs in 40% of cases.[12] However, donor conversion

Key words
- Aneurysm
- Brain death
- Conversion rate
- Irreversible total loss of brain function
- Organ donation
- Subarachnoid hemorrhage

Abbreviations and Acronyms
aSAH: Aneurysmal subarachnoid hemorrhage
ICU: Intensive care unit
ILBF: Irreversible loss of brain function

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rates vary not only among different pathologies leading to ILBF but also among countries as well as within regional areas in these countries.[13-15] Various factors, such as age, sex, ethnicity, and language,[13,16] influence the rate of consent for organ donation. In this study, we assessed the prevalence of ILBF in patients with aSAH and analyzed the rate of conversion to organ donation as well as the overall approval rate of relatives. In addition, we assessed demographic and clinical parameters affecting eligibility and consent for organ donation.

MATERIALS AND METHODS

This study was reported to the local ethics council (WF-01/17). From January 2011 to December 2016, 395 patients with aSAH were referred to our university medical center. In 2016, approximately 130 patients were admitted for elective aneurysm treatment, thus constituting our center a high-volume neurovascular center. Of 395 patients with aSAH, 71 died and were further retrospectively analyzed. Baseline parameters for age, sex, initial Glasgow Coma Scale score,[17] Hunt and Hess grade,[18] World Federation of Neurosurgical Societies score,[19] Fisher grade,[20] presence of aneurysmal rebleeding, intracerebral hemorrhage, location of aneurysm, treatment, signs of herniation, Simplified Acute Physiology Score II,[21,22] and length of ICU stay until ILBF was diagnosed were recorded. Aneurysmal rebleeding was categorized as rebleeding before admission and/or treatment of aneurysm, during treatment of aneurysm, or after treatment of aneurysm. Finally, we analyzed the organ donor conversion rate and assessed how many organs could be transplanted. Localization of aneurysms was distributed into 2 groups as described before by our study group.[23] Initial signs of herniation were defined as an anisocoria or as unilateral or bilateral fixed and dilated pupils with missing reaction to light.

Local Organ Donation Guidelines

In Germany, legal conditions for organ transplantation are regulated by the German Transplant Law,[24] and the diagnosis of ILBF is regulated by the guidelines of the German Medical Association.[25] The German Organ Transplantation Foundation (Deutsche Stiftung Organtransplantation) is officially assigned the role of organ procurement agency and is responsible for coordinating the organ donation procedure. ILBF must be diagnosed by 2 independent consultants with >2 years of experience in the treatment of critically ill patients with brain damage. At least 1 of the physicians must be a board certified neurologist or neurosurgeon. With evidence of an acute catastrophic brain pathology that is compatible with the clinical diagnosis of ILBF, after exclusion of confounding pathologies (i.e., electrolyte and acid-base disturbances, hypoglycemia, circulatory shock, hypothermia, or drug intoxication including the accumulation of sedative drugs), both physicians must examine the patient. With absent brainstem reflexes, an apnea test is performed requiring no spontaneous breathing until a temperature-corrected arterial partial pressure of carbon dioxide of at least 60 mm Hg (8 kPa). Special tests apply for patients with a chronically elevated partial pressure of carbon dioxide (e.g., as in chronic obstructive pulmonary disease). For supratentorial brain damage in adults, irreversibility of ILBF may be verified either after a second set of clinical examinations after 12 hours of observation time for primary brain damage or 72 hours for secondary brain damage or immediately after ancillary testing (i.e., electroencephalography confirming an isoelectric line for at least 30 minutes or detection of cerebral circulatory arrest). For infratentorial brain damage, ancillary testing is mandatory.

After confirmation of ILBF, the patient's willingness to donate organs is evaluated. In the absence of an organ donor card, the patient's spouse, the closest relative, or a legal surrogate is interviewed about the patient's assumed will and may then give or decline consent for organ donation. To further optimize the allocation of the harvested organs, the German Organ Transplantation Foundation registers donors during the preparation of organ donation with the Eurotransplant International Foundation (Leiden, The Netherlands; www.eurotransplant.org), which allocates donor organs within the participating countries (Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, The Netherlands, and Slovenia).

Statistical Analysis

IBM SPSS Statistics for Windows Version 24 (IBM Corp., Armonk, New York, USA) was used for statistical analysis. Routine cross table, χ^2, and t tests were used for baseline data evaluation. Significant factors impacting organ donation rates were identified after dichotomization (comparing "decline" vs. "consent" for organ donation) using a χ^2 test. A P value <0.05 was defined as level of significance. All data were tested for normality with the Shapiro-Wilk test. The data are presented as mean ± SD or as median and interquartile range as appropriate. Graphic analysis was performed using SigmaPlot Version 13.0 (Systat Software, Inc., San Jose, California, USA), Microsoft Excel 2010 (Microsoft Corp., Redmond, Washington, USA), and GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, California, USA).

RESULTS

Patient Characteristics

Within the 5-year time frame, we treated 395 patients for aSAH at our institution. The acute mortality rate was 18.0%, with 71 patients who died as a result of complications of aSAH (**Figure 1**). Baseline demographic and clinical parameters are presented in **Table 1**. In 20 (28.2%) patients, further treatment in the ICU was stopped owing to patients' supposed refusal of an ICU treatment in critical illness with a high risk of severe disabilities. When clinical signs of ILBF were documented, 13 (18.3%) relatives, although in knowledge of the patient's supposed will, refused to approve performance of the diagnosis pathway for ILBF. In 2 (2.8%) cases, an organ donation was not possible because of a known metastatic cancer.

Diagnosis of ILBF

ILBF was documented in 36 patients (50.7%). After clinically suspicious signs of ILBF were noted, it took 62.8 hours ± 28.0 (range, 13.75–127.68 hours) until ILBF was confirmed. In 55.6% of all ILBF cases ($n = 20$), an additional diagnostic tool was needed to confirm ILBF. In all these cases, electroencephalography was chosen to confirm ILBF. A second clinical examination was performed in the remaining 16 patients (44.4%).