ABSTRACT

Purpose While most research focuses on the association between medical characteristics and residual morbidity of survivors of the acute respiratory distress syndrome (ARDS), little is known about the relation between potentially modifiable intensive care unit (ICU) features and the course of health-related quality of life (HRQoL). Accordingly, the DACAPO study was set up to elucidate the influence of quality of intensive care on HRQoL and return to work (RtW) in survivors of ARDS. The continued follow-up of these former ICU patients leads to the establishment of the DACAPO (survivor) cohort.

Participants Sixty-one ICUs all over Germany recruited patients with ARDS between September 2014 and April 2016. Inclusion criteria were: (1) age older than 18 years and (2) ARDS diagnosis according to the ‘Berlin definition’. No further inclusion or exclusion criteria were applied. 1225 patients with ARDS could be included in the DACAPO ICU sample. Subsequently, the 876 survivors at ICU discharge form the actual DACAPO cohort.

Findings to date The recruitment of the participants of the DACAPO cohort and the baseline data collection has been completed. The care-related data of the DACAPO cohort reveal a high proportion of adverse events (in particular, hypoglycaemia and reintubation). However, evidence-based supportive measures were applied frequently.

Future plans Three months, 6 months and 1 year after ICU admission a follow-up assessment is conducted. The instruments of the follow-up questionnaires comprise the domains: (A) HRQoL, (B) RtW, (C) general disability, (D) psychiatric symptoms and (E) social support. Additionally, an annual follow-up of the DACAPO cohort focusing on HRQoL, psychiatric symptoms and healthcare utilisation will be conducted. Furthermore, several add-on projects affecting medical issues are envisaged.

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many ARDS survivors suffer from long-term persistent physical and mental morbidity. A systematic review with subsequent meta-analysis revealed lower pooled estimated scores for all health-related quality of life (HRQoL) domains of the Medical Outcomes Study Short Form 36-Item Health Survey in ARDS survivors compared with general population. Even 5 years after ICU discharge, ARDS survivors have decreased HRQoL and a reduced 6min walk distance compared with mean norm scores. Among the mental disorders, increased prevalence rates are reported for depression, post-traumatic stress disorder (PTSD) and anxiety disorder in former patients with ARDS. Taken together, there is a growing body of evidence for decreased HRQoL and disability, but little is known about determinants of clinical relevance for HRQoL and return to work (RtW) in survivors of ARDS.

Furthermore, none of the large ARDS cohorts provide sufficient information on sociodemographic characteristics of patients with ARDS and ARDS survivors. Against this background, an ARDS survivor cohort that allows investigation into the influences of hospital quality of care (QoC) and subsequent healthcare utilisation (HCU) on prolonged mental and physical morbidity, HRQoL and RtW is highly desirable.

**COHORT DESCRIPTION**

A sample of ARDS survivors in German ICUs has been selected within the scope of the DACAPO study (‘DACAPO: Surviving ARDS: the influence of quAlity of Care and individual Paient characteristics on quality Of life’ funded by German Federal Ministry of Education and Research). The main objective of this study is to investigate the influence of QoC on HRQoL and RtW. With respect to the association between QoC and HRQoL/RtW, further hypotheses regarding moderating effects of sex, socioeconomic status, social support and psychopathological symptoms should be tested. A detailed protocol of the study has been published previously.

By conducting additional follow-ups every 12 months after discharge from ICU, this initial sample will be transformed into the DACAPO (survivor) cohort. In particular, the DACAPO cohort will be set up to facilitate research in HCU and long-term psychiatric morbidity among ARDS survivors and to analyse long-term effects of QoC and HCU on HRQoL.

Between September 2014 and May 2016, 61 ICUs all over Germany included eligible patients with ARDS in the DACAPO ICU sample. Efforts were made to ensure that not only hospitals/ICUs specialised in the treatment of patients with ARDS (members of the ARDS Network Germany) participate, by reaching out to smaller urban or suburban hospitals. All participating clinics declared their willingness to include all eligible patients in the cohort during the period of recruitment. Written informed consent had to be provided by the patient. In patients who were cognitive incapable informed consent of patients’ caregivers or legal guardians needed to be obtained.

Eligible patients had to meet following criteria for inclusion in the DACAPO ICU sample:

- ARDS is diagnosed in one of the participating ICUs or a referring hospital according to the ‘Berlin definition’.
- Patient is older than 18 years at ARDS diagnosis.

In order to ensure maximal external validity of the DACAPO ICU sample, no further inclusion criteria and no exclusion criteria were applied.

The actual DACAPO cohort consists of the survivors of the DACAPO ICU sample (patients who were discharged alive from the ICU).

**Measurements**

During ICU treatment, a wide variety of sociodemographic, disease-related and care-related characteristics were recorded. Data acquisition was performed by means of web-based electronic case report forms (eCRFs). For this purpose, study nurses and physicians of every participating hospital were trained with regard to the detailed specification of the data that should be collected and the operation of the eCRFs.

Along with two short-term follow-up assessments (3 months and 6 months after ICU discharge), a yearly follow-up assessment is in progress.

Each follow-up consists of a paper–pencil questionnaire that is sent by post to the participant’s home address. In order to minimise drop-out rates, we routinely mail a reminder letter and place a reminder phone call asking participants to complete and sent back the questionnaire. If there is no response to the reminder letters and reminder calls, we get in touch with the local resident registration office to receive information about whether the participant has died (mortality follow-up) or moved to another address.

**Exposure**

QoC is assessed in all participating ICUs. In cases where ARDS has been diagnosed in a referring hospital, QoC has been determined for the referring ICU as well. For this purpose, we apply the indicators of the quality assurance programme for intensive care implemented by the Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin (German Interdisciplinary Association for Intensive and Emergency Medicine). These indicators are situated at the level of process and structural quality. In addition to this generic quality of intensive care indicator set, several ARDS specific variables have been incorporated. All indicators will be assessed by questionnaire at the institutional level.

If applicable, QoC was assessed on individual patient level for the interhospital transport between the referring hospitals and the participating ICUs. Particular attention was paid to indicators regarding process quality (medical equipment of the vehicle and medical qualifications of personnel).
An important issue to be investigated based on the data of the DACAPO cohort is the long-term effects of HCU on HRQoL and RtW. Therefore, the follow-up questionnaires (starting from the 6-month follow-up) include questions regarding utilisation of ambulatory, inpatient and rehabilitative healthcare services.

**Follow-up: outcomes**

The primary outcome is assessed by the Short Form-12 self-report questionnaire (SF-12), which has two scales (one for physical health and one for mental health). The secondary outcome RtW is determined by several items relating to date and extent of RtW.

**Follow-up: moderator variables and covariates**

With regard to a valid assessment of morbidity and disease severity, several scores for morbidity and disease severity (Simplified Acute Physiology Score (SAPS) II, SAPS III, Sequential Organ Failure Assessment (SOFA) score) have been recorded on item level for every patient at the time of (1) admission, (2) diagnosis of ARDS, (3) 24 hours after diagnosis and (4) discharge from ICU. For the sociodemographic characterisation age, gender, marital status, educational and professional level, living condition and socioeconomic status have been captured based on the information of the relatives/legal guardians. In addition, medical/supportive treatment (ECMO, tracheotomy, nitric oxide inhalation, prone positioning and neuromuscular blockers) and adverse events (hypoglycaemia, hypoxia, accidental extubation and reintubation) have been assessed on individual patient level. In particular, most of the variables recorded in the phase of ICU treatment are intended to be covariates for the adjustment of disease severity, comorbidity and socioeconomic status in the final statistical model determining the influence of QoC on HRQoL and RtW. In addition, these medical baseline data (possibly combined with the exposure and/or outcome measurements) can serve as database for future clinical epidemiology research.

**ICU baseline: moderator variables and covariates**

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**CHARACTERISTICS OF STUDY PARTICIPANTS**

Overall, 1900 patients with ARDS were enrolled in the electronic data capture system. Informed consent was obtained by 1225 of the patients or their legal guardians. The 876 ARDS survivors at the time of ICU discharge form the actual DACAPO cohort. A diagram of the patient flow is provided in figure 1. Descriptive statistics of sociodemographic and medical characteristics at the time of admission for the entire DACAPO ICU sample and for the DACAPO cohort (ICU survivors) are presented in table 1. Small to moderate numbers of missing data in the medical variables are attributable to the
fact that many of the clinical and care-related characteristics are routinely recorded in the ICU setting.

Findings to date
The distribution of sex and age in our cohort is in perfect accordance with other large ARDS cohorts, which reveal that in particular older men are at higher risk for ARDS. Furthermore, the high prevalence of pulmonary diseases including pneumonia as most important risk factor of ARDS is in line with the scientific literature in this area.12

Taking a closer look at critical events (hypoxia, hypoglycaemia, unintended extubation and reintubation) and supportive measures (tracheotomy, NO inhalation, ECMO, prone positioning and neuromuscular blockers) during ICU treatment, in particular the application of ECMO and prone positioning, were frequent, whereas critical events like hypoglycaemia also had a high prevalence.12 These findings point out the potential for improvement in intensive care routines. However, the results reveal a comprehensive implementation of evidence-based measures like prone positioning25 26 and neuromuscular blockers.27

Against the background of changing diagnostic ARDS criteria, further comparisons of medical characteristics and outcomes between studies/cohorts should

Table 1

<table>
<thead>
<tr>
<th>Selected baseline sociodemographic and medical characteristics of the DACAPO ICU sample and of the ICU survivors (initial DACAPO cohort)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DACAPO ICU sample</strong></td>
</tr>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
</tr>
<tr>
<td>Sex (N)</td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td>Age (N)</td>
</tr>
<tr>
<td>Years, Md (IQR)</td>
</tr>
<tr>
<td>Educational level* (N)</td>
</tr>
<tr>
<td>No school leaving certificate, n (%)</td>
</tr>
<tr>
<td>Not yet a school leaving certificate, n (%)</td>
</tr>
<tr>
<td>Schooling &lt;10 years</td>
</tr>
<tr>
<td>Secondary school leaving certificate, n (%)</td>
</tr>
<tr>
<td>Schooling=10 years</td>
</tr>
<tr>
<td>Intermediate school leaving certificate, n (%)</td>
</tr>
<tr>
<td>Schooling &gt;10 years</td>
</tr>
<tr>
<td>University entrance level, n (%)</td>
</tr>
<tr>
<td>Unknown or other n (%)</td>
</tr>
<tr>
<td><strong>Medical characteristics</strong></td>
</tr>
<tr>
<td>SAPS-II†‡§ score (N)</td>
</tr>
<tr>
<td>Md (IQR)</td>
</tr>
<tr>
<td>SOFA‡§ score (N)</td>
</tr>
<tr>
<td>Md (IQR)</td>
</tr>
<tr>
<td>Cause of ARDS (N)</td>
</tr>
<tr>
<td>Pulmonary, n (%)</td>
</tr>
<tr>
<td>Extrapulmonary, n (%)</td>
</tr>
<tr>
<td>Not specified, n (%)</td>
</tr>
<tr>
<td>Severity of ARDS§ (N)</td>
</tr>
<tr>
<td>Mild, n (%)</td>
</tr>
<tr>
<td>Moderate, n (%)</td>
</tr>
<tr>
<td>Severe, n (%)</td>
</tr>
</tbody>
</table>

Note: numbers do not add up to n=1225 for all patients or to n=876 for survivors due to missing values.
*Data were provided by patients’ caregivers/legal guardians.
†As assessed at admission at the DACAPO ICU.
‡As assessed at time of ARDS diagnosis.
§SAPS-II score was calculated without the Glasgow Coma Scale.
ARDS, acute respiratory distress syndrome; ICU, intensive care unit; Md, median; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment.
be drawn with caution. The Large observational study to UNderstand the Global impact of Severe Acute respiratory Failure (LUNG SAFE) provides currently the only reliable sample of patients with ARDS corresponding to the current criteria of the ‘Berlin definition’. The distribution of ARDS severity revealed by the LUNG SAFE sample differs from our findings. While LUNG SAFE reports the lowest proportion of persons with severe ARDS, the baseline data of our investigation indicate a much higher proportion of patients with severe ARDS and a lower proportion of patients with mild ARDS, but nevertheless the overall ICU mortality rate (28.4%) is lower in our DACAPO ICU sample.

Strengths and limitations
One of the strengths of the DACAPO cohort is the characterisation of ARDS survivors with a particular focus on sociodemographic conditions (education, socioeconomic status, marital status and so on). With regard to information bias, only validated instruments with satisfying psychometric properties are applied for psychometric constructs. A further strength is the broad spectrum of hospitals respectively ICUs that participated in patient recruitment. We were successful in involving university hospitals providing up-to-date apparatus and optimal personnel resources as well as smaller urban and suburban hospitals. This approach should reduce selection bias and ensure external validity. Additionally, in order to draw a representative sample/coh0rt of the general population of ARDS survivors, no exclusion criteria were applied. However, the sample of the participating ICUs was drawn following a convenience sampling method, and the distribution of ARDS severity in the DACAPO ICU sample is not in accordance with the only large study applying the current Berlin definition of ARDS. The latter point tends to indicate that, although physicians of the participating ICUs have been trained in applying the diagnostic ARDS criteria of the Berlin definition, the mild form of ARDS is frequently overlooked in intensive care routine. This, in turn, would lead to a loss of representativeness of the DACAPO cohort and points out the need to screen all patients for eligibility in order to ensure representativeness, in particular if empirical and consensus-based and, therefore, non-salient syndromes like ARDS are investigated. Against this background, a strict implementation

Figure 2 Main objectives and add-on projects using data of the DACAPO ICU sample/DACAPO cohort. (I) Main objective of the DACAPO study; (II) main objective of the DACAPO cohort; (III) genetic add-on project; and (IV) add-on projects with clinical background. An additional DNA analysis for the participants of the DACAPO cohort is intended. For some of the research questions, a retrospective collection of medical data is required. An additional follow-up with specific measurement instruments is intended for some research questions. ARDS, acute respiratory distress syndrome; HRQoL, health-related quality of life; HCU, healthcare utilisation; ICU, intensive care unit; PTSD, post-traumatic stress disorder; QoC, quality of care; RTW, return to work.
of an entity apart from the daily clinical routines that conducts the screening process every day would have been expedient. Because of the considerable number of participating ICUs, this approach was not feasible in practice.

Nevertheless, the DACAPO cohort is one of the largest cohorts of ARDS survivors described in literature and should be suitable for analytical issues related to associations between QoC, disease-related or care-related patient characteristics and physical, mental or social difficulties at the follow-up evaluations. At the same time, the DACAPO cohort enables taking into consideration important aspects of the individual sociodemographic conditions.

Collaborations

On the basis of a regulation given by the principal investigators of the study, every participating ICU that included at least one patient is encouraged to propose research questions that could be examined using the data provided by the DACAPO ICU sample, the DACAPO cohort and the data of the assessment of QoC. Figure 2 provides an overview of the main objective of the DACAPO study and envisaged projects going beyond.

The aim of a genetic add-on project is to investigate in ARDS survivors whether (1) there is an association between the NF-xB1 (−94 ins/del ATTG) promoter polymorphism and HRQoL and/or RW and whether (2) the C957T polymorphism of dopamine D2 receptor gene and a single nucleotide polymorphism in SLC18A2 (rs363276) are associated with increased incidence of PTSD. Therefore, a DNA analysis of the DACAPO cohort participants using oral mucosa swabs is intended.

Furthermore, several add-on projects concerned with clinical topics of high relevance are currently under preparation. For some of these projects, the retrospective collection of additional medical ICU variables on individual patient level is required. For other research questions, an adapted follow-up questionnaire with additional measurement instruments (dysphagia, chronic pain and so on) has to be conducted (see figure 2). For details regarding the availability of data for potential new collaborators, see the data sharing section.

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Contributors FD-S analysed, interpreted the data and wrote the manuscript; SuB helped writing the manuscript and also reviewed it for important intellectual content; MB, SaB, MQ, SW-C, SK, TK, TM, SvB, BE, ChristianAv, PM, MA, AG and CK reviewed the manuscript for important intellectual content; TB contributed his knowledge and expertise in the field of intensive care and reviewed the manuscript for important intellectual content; ChristianAp helped in writing the manuscript and reviewed it for important intellectual content. All authors have read and approved the final version of the manuscript.

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Ethics approval Ethics Committee of the University of Regensburg.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES


17. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems


