Impact of the Advanced Practice Provider in Adult Critical Care: A Systematic Review and Meta-Analysis*

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Objectives: To evaluate the effects on quality and efficiency of implementation of the advanced practice provider in critical care.

Data Sources: PubMed, Embase, The Cochrane Library, and CINAHL were used to extract articles regarding advanced practice providers in critical care.

Study Selection: Articles were selected when reporting a comparison between advanced practice providers and physician resident/fellows regarding the outcome measures of mortality, length of stay, or specific tasks. Descriptive studies without comparison were excluded. The methodological quality of the included studies was rated using the Newcastle-Ottawa scale. The agreement between the reviewers was assessed with Cohen's kappa. A metaanalysis was constructed on mortality and length of stay.

Data Extraction and Synthesis: One-hundred fifty-six studies were assessed by full text. Thirty comparative cohort studies were selected and analyzed. These compared advanced practice providers with physician resident/fellows. All studies comprised adult intensive care. Most of the included studies showed a moderate

*See also p. 737.

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to good quality. Over time, the study designs advanced from retrospective designs to include prospective and comparative designs. **Data Synthesis:** Four random effects meta-analyses on length of stay and mortality were constructed from the available studies. These meta-analyses showed no significant difference between performance of advanced practice providers on the ICU and physician residents/fellows on the ICU, suggesting the quality of care of both groups was equal. Mean difference for length of stay on the ICU was 0.34 (95% Cl, -0.31 to 1.00; $l^2 = 99\%$) and for in hospital length of stay 0.02 (95% Cl, -0.85 to 0.89; $l^2 = 91\%$); whereas the odds ratio for ICU mortality was 0.98 (95% Cl, 0.81-1.19; $l^2 = 37.3\%$) and for hospital mortality 0.92 (95% Cl, 0.79-1.07; $l^2 = 28\%$).

Conclusions: This review and meta-analysis shows <u>no differences</u> <u>between acute care given by advanced practice providers compared with physician resident/fellows</u> measured as length of stay or mortality. However, advanced practice providers might add value to care in several other ways, but this needs further study. (*Crit Care Med* 2019; 47:722–730)

Key Words: acute care nurse practitioner; advanced practice provider; intensive care unit; nurse practitioner; physician assistant; quality of care

For more than 2 decades, acute care nurse practitioners (ACNPs) and physician assistants (PAs) are increasingly embedded in ICUs, particularly in the United States (1, 2). However, in the rest of the world, this concept remains relatively unknown, despite the fact that research about the additional value of this concept continues to emerge. This systematic review and meta-analysis established an overview about the current available evidence in this area.

Nowadays, hospital care is challenged by several trends such as an increasing demand in efficiency and quality of healthcare, a rising proportion of patients with chronic diseases and ongoing specialization in medical disciplines. This often coincides with increasing physician shortages in several regions in the world (3–6). In light of these developments, one of the applied solutions has been to reallocate patient care to PA and

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nurse practitioners (NPs) also called "advanced practice provider" (APP). An APP is a nonphysician with an independent license to practice as APP. APPs, in collaboration with healthcare professionals and other individuals, provide a full range of primary, acute, and specialty healthcare services.

This staffing model shows beneficial outcomes and has gained popularity within various medical disciplines, like surgical and trauma teams, but also in pediatric and adult ICUs (1, 2, 7–9). Except for the United States where APPs were already legalized during the 1960s (10–12), they are currently increasingly recognized and adapted by other countries in the world and in the critical care processes of these countries (3, 4). In the last years, several reviews were undertaken to assess the added value of the critical care APP to clinical teams and the exact role of this APP (7, 13-16). The review of Woo et al (16) highlighted that APPs can increase patients' access to emergency and critical care and showed that APPs improve patient outcomes. The review of Fry (15) also demonstrated that the available evidence about APPs showed a contribution to positive patient, service, and nursing outcomes. In addition, organizational models with APPs seem to be cost-effective, appropriate, and efficient in delivery of critical care services. It was recognized that health systems and the role of APPs differs between countries and studies in specific local situations are needed (15). The reviews of Edkins et al (14), Gershengorn et al (13), and Kleinpell et al (7) showed promising results regarding embedding of APPs in critical care. However, all review articles came to the same conclusion that the literature was mainly descriptive and not solid enough for definite conclusions.

The objective of this systematic review and meta-analysis is to gain insight in the place and additional value of the APPs in critical care and to investigate the quality and efficiency of care provided by APPs compared with physicians.

METHODS

A systemic literature review was conducted till July 2018, observational studies or randomized controlled trials were included if these studies reported the quality of care in critical care provided by APPs, physician residents/fellows, or attending physicians. Studies were eligible for inclusion when they described adults (\geq 18 yr old) admitted to the ICU. In addition, the outcome data should be sufficiently described to be graded and compared. Data on mortality, ICU or length of stay (LOS), and the outcome of specific skills like insertions of IV catheters or communication skills, had to be reported. Exclusion criteria were studies in which the minimal data set for grading was absent, such as descriptive letters or poster abstracts. Studies performed on neonatal ICUs, written in another language than English or Dutch, and studies without full text available were also excluded.

Search Strategy

PubMed, Embase, The Cochrane Library, and CINAHL were searched from the earliest date of each database up to

July 2018 with the following keywords that were modified to suit each database: critical, care, unit, units, intensive, acute, nonphysician, provider, nurse, physician, assistant (**Table S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/ E385). The references from selected articles were manually searched to include references that were thought being eligible for inclusion.

Study Selection and Data Extraction

Authors (H.G.K., S.P.) independently screened and included studies based on the retrieved titles and abstracts. The same two authors reviewed then the full text of the selected studies and determined suitability for inclusion, based on the established selection criteria. For further eligible studies, cross-references were screened. Disagreements were resolved by discussion and consensus with each other, author (A.d.B.) and senior author (P.v.d.V.).

All relevant data were independently extracted (by H.G.K., A.d.B.) and subsequently verified (by P.v.d.V.).

Assessment of Quality

The Newcastle-Ottawa scale (NOS) was used to assess the methodological quality of the included nonrandomized studies (17). Two authors (H.G.K., A.d.B.) performed this assessment separately. This 9-point scale is based on three domains: 1) selection of the cohort, 2) comparability of the groups, and 3) quality of the outcomes. High-quality studies have a score of greater than or equal to 7, whereas moderate- and low-quality studies have scores of 4–6 and less than or equal to 4.

Statistical Analysis

The level of agreement of the independently scored NOS between the two authors was assessed by a Cohen's kappa score. A Cohen's kappa of less than 0.20 was considered as poor agreement, 0.21–0.40 as fair agreement, 0.41–0.60 as moderate agreement, 0.61–0.80 as good agreement, and 0.81–1.00 as very good agreement (18).

Meta-analyses were performed when more than three studies with comparable design and sufficient data were available. To avoid bias, we only included studies comparing two distinct groups of APPs and physicians. All meta-analyses were performed with the open-source software Openmetaanalyst (Brown University, Center for Evidence Synthesis in Health, School of Public Health, Providence, RI) (19). Adjusted outcome data were used when available. No structural risk of bias assessment was performed. Data reported as medians were converted to means with sDs according to the method described by Luo et al (20). A DerSimonian and Laird random-effects models were used to pool the dichotomous data while the weighted mean difference with 95% CIs was used for continuous data. Hedges "g" was used for the pooled sample variance. Statistical heterogeneity was examined using the Cochran's test and P statistic. Values of p less than 0.05 were considered statistically significant. Statistical Package for Social Sciences (SPSS, Chicago, IL; Version 20.0) was used to prepare the database and for statistical analysis.

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RESULTS

The Preferred Reporting Items for Systematic Reviews and Metaanalyses flowchart in **Figure 1** demonstrates the search results. The initial database search produced 11,643 results, including 3,364 duplicates. After screening on title and abstract, 156 studies were considered relevant for a full text critical appraisal. A total of 126 studies were excluded due to deficient data reporting. Thirty studies were included in this systematic review, whereas eight studies were suitable for the meta-analyses (21–28).

Study Quality

A Cohen's kappa of 0.69 reflected a good agreement between authors (H.G.K., A.d.B.). **Table 1** describes the NOS assessment of the methodological quality for the included studies

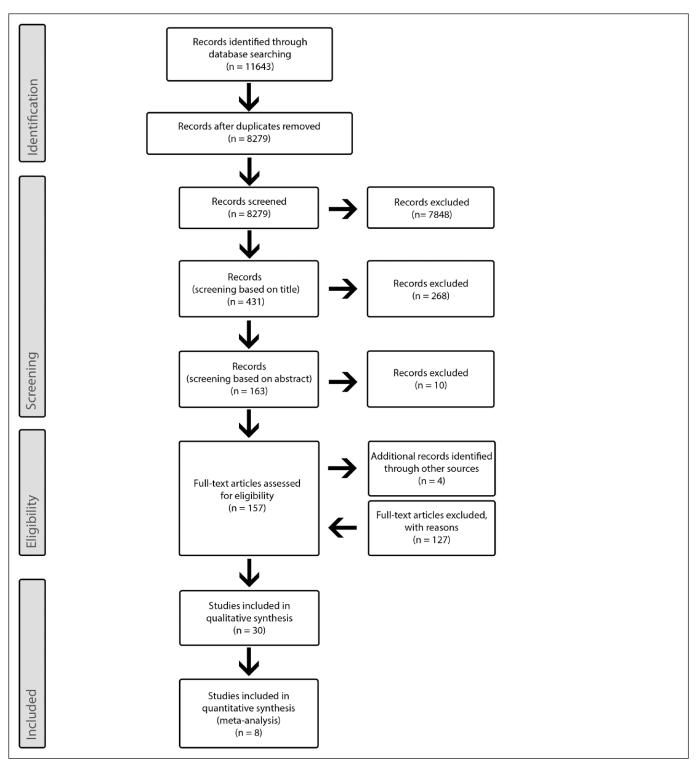


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flowchart.

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TABLE 1. Assessment of Methodological Quality Using the Newcastle-Ottawa Scale

	Newcastle-Ottawa Scale Results			
References	Selection (4)	Comparability (2)	Outcome (3)	Total (9)
Alexandrou et al (29)	2	0	3	5
Alexandrou et al (30)	2	0	3	5
Bevis et al (31)	4	0	3	7
Burns et al (32)	4	0	2	6
Butler et al (33)	4	0	1	5
Christmas et al (34)	4	0	2	6
Collins et al (35)	4	0	2	6
Costa et al (36)	4	2	3	9
Dubaybo et al (27)	4	0	2	6
Gershengorn et al (25)	4	2	3	9
Gershengorn et al (37)	4	2	3	9
Gillard et al (28)	4	1	2	7
Gracias et al (38)	3	0	2	5
Hoffman et al (39)	4	2	3	9
Hoffman et al (22)	4	2	2	8
Hoffman et al (40)	4	2	2	8
Jefferson and King (41)	4	2	3	9
Kapu et al (42)	4	2	3	9
Kawar and DiGiovine (23)	4	2	3	9
Landsperger et al (21)	4	2	3	9
Matsushima et al (43)	4	2	3	9
Pirret (44)	4	0	2	6
Rayo et al (45)	4	0	2	6
Rudy et al (26)	3	0	3	6
Russell et al (46)	3	0	2	5
Scherzer et al (24)	4	2	3	9
Sidani et al (47)	4	0	2	6
Sirleaf et al (48)	3	0	2	5
Skinner et al (49)	4	1	2	7
van Vught et al (50)	4	2	3	9

per author. Sixteen studies were assessed as high quality with 11 studies reaching the maximum score of 9 (Table 1). Fourteen studies were assessed as moderate quality (Table 1).

Summary of Studies

A total of 30 cohort studies were included of which 13 were retrospective, 13 were prospective and four were mixed cohort studies in which prospective data were compared with a retrospective obtained baseline situation. An overview of the studies is depicted in **Table S2** (Supplemental Digital Content 2, http://links.lww.com/CCM/E386). The studies compared ACNPs or acute care PAs to physician residents, fellows, or for some instances attending physicians. This was done by measuring the performance of separate APP groups to physician resident/fellows or by comparing mixed groups with physician resident/fellows and added APPs to a situation without APPs. The only uniform and comparable studies to create a metaanalysis were the studies which compared ICU care of APPs with that of physician residents/fellows. Four meta-analyses were constructed from the available studies which showed no

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significant difference between performance of APPs on the ICU and physician residents/fellows on the ICU suggesting the quality of care of both groups was equal.

APP on the ICU

Mortality

Ten studies reported mortality data in the ICU or both in the ICU and hospital. Six studies had a prospective observational cohort design (21, 22, 26, 40, 43, 49) and four had a retrospective observational cohort design (23-25, 36). Six studies reported on ICU mortality (21-24, 40, 49) and seven studies reported on hospital mortality (21, 23, 25, 26, 32, 36, 43). One study (40) was a subgroup of another larger study (22). Of the prospective mortality studies, four (21, 22, 40, 49) analyzed ICU mortality, three by measuring the results of a combined team of physician resident/fellows and APPs and one, the study of Landsperger et al (21), compared the results of an ICU run by ACNPs and an ICU run by physician residents, both with intensivist oversight. This study showed a significant difference in ICU mortality in favor of ICUs run by ACNPs in conjunction with an intensivist. Hospital mortality was not significantly different. All other prospective studies showed no difference between APPs and physician resident/fellows.

Of the retrospective studies, two reported about ICU mortality (23, 24). All these retrospective studies reported an equal mortality when comparing APPs with physician resident. In the pooled analysis, the subgroup analysis of Hoffman et al (40) was excluded because data had already been reported to some extend and the study of Skinner et al (49) was excluded because it provided insufficient data.

In the studies measuring hospital mortality, the study of Costa et al (36) was the largest study and investigated 29 medical and mixed medical-surgical ICUs in 22 hospitals with teams with and without APPs. The risk-adjusted hospital mortality was similar between the groups. Due to the survey design of this study and therefore possible biased results, we excluded this study in the meta-analysis. The other six studies reported no differences in hospital mortality. The study of Matsushima et al (43) which reported on a work scheme change of APPs instead of the addition of new APPs were also excluded. Unadjusted data with adjusted data, if available, showed no 43, 46). Seven of these were prospective cohort studies (21, 22, 26, 32, 40, 43, 46) and five were retrospective cohort studies (23–25, 27, 28). Three of the prospective studies compared the ICU LOS of ACNP-staffed ICUs with physician resident/fellows staffed ICUs with both groups being supervised by an attending intensivist (21, 22, 40). All these three studies showed no significant difference of ICU LOS between both groups. One study compared a work scheme change where NPs were implemented in night shifts (43). The other studies compared either implementation of APPs in a physician resident/fellows team or the outcomes of specific patients groups cared for by ACNPs.

The difference in ICU LOS in the five retrospective studies varied. When four midlevel practitioners were added in a trauma service which included ICU care, the ICU LOS decreased (4.08 d [sD, 0.27 d] vs 3.28 d [sD, 0.20 d]) (28). In contrast, two other studies found a longer ICU LOS when patients when APPs were implemented. In one study, the authors attributed the difference to baseline characteristics (the assumption was more chronically ill patients were included in the NP group) and to discharge location (mean 7.9 d [sD, 7.5 d] vs 5.6 d [sD, 6.5 d]) (24). The other study, that did not adjust for confounders, reported a longer ICU LOS for patients on PA-staffed ICUs compared with physician resident/fellows staffed ICUs without explanation (mean 3.96 d [sD, 0.92 d] vs 4.62 d [sD, 1.91 d]) (27). The last two of the five retrospective studies reported no significant difference of ICU LOS after adjustment for confounders. In the pooled analysis, four studies were excluded. Matsushima et al (43) and Hoffman et al (40) were excluded because one was a subgroup analysis of another included study and one was a work scheme change. The study of Burns et al (32) was excluded because it reported on implementation of an outcome manager which supervised protocol adherence. The study by Russell et al (46) was excluded because the study provided insufficient data.

Nine studies reported hospital LOS (21, 23–26, 28, 32, 43, 46). Five studies were prospective cohort studies (21, 26, 32, 43, 46) and four studies were retrospective cohort studies (23–25, 28). One study reported on hospital mortality using a work scheme change of the APPs. This did not result in changes in hospital LOS. The study did not differentiate between patients treated by APPs or physician resident; therefore, it was not included in the meta-analysis. Only the prospective study of Landsperger et

significant difference for ICU mortality (odds ratio [OR], 0.98; 95% CI, 0.81–1.19; p = 0.04; $l^2 = 37.3\%$) and hospital mortality (OR, 0.92; 95% CI, 0.79–1.07; p = 0.33; $l^2 = 28\%$) between both groups (**Fig. 2**, data on hospital mortality not shown). The figures report the studies with adjustment for confounders.

LOS

Twelve studies report about the ICU LOS with an APP present on the ICU (21–28, 32, 40,

Odds Ratio Studies 95% CI APP Physicians Ν Ν Events Weight OR 95% CI Year Events Hoffman 2005 9.14% 250 276 26 22 1.34 [0.74 - 2.43] 159 34.88% Kawar 2011 1249 177 1249 1.13 [0.90 - 1.42 Scherzer 221 936 16.21% 0.74 - 1.70 2017 32 123 1.12 Landsperger* 2016 2366 N.A 6700 N.A 39.77% 0.77 [0.63 - 0.94] 0.98 [0.81 - 1.19] Total 4086 9161 (S.E.=0.1, p=0.87)0.01 1.5 Heterogeneity: 0.5 2 Tau²= 0.01, Cohran's Q= 8,35, df= 3, I²= 37.29, p= 0.04 Favors Physician * numbers were not available due to adjustment

Figure 2. ICU mortality. APP = advanced practice provider, df = degrees of freedom, N.A. = not applicable.

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al (21) compared ACNP-staffed ICUs with physician resident staffed ICUs, both with attending physician oversight, and also adjusted for confounders. This study reported a significant lower hospital LOS for patients who were admitted on ACNP-staffed ICUs (OR, 0.87; 95% CI, 0.80–0.95; p = 0.001). The prospective study of Rudy et al (26) with a similar design did not report a significant difference but lacked adjusting for confounders. The other two prospective studies by Burns et al (32) and Russell et al (46) implemented APPs to supervise treatment of patients via specific protocols. Both studies showed a significant reduction of hospital LOS when the ACNP was implemented, but there was insufficient data available to include them in the meta-analysis.

Of the four retrospective cohort studies, one study was the earlier mentioned implementation of four additional midlevel practitioners with an associated reduction in Hospital LOS (5.09 d [sd, 0.20 d] vs 4.84 d [sd, 0.20 d]) (28). Because not all patients received ICU care, the results do not solely reflect the APP in critical care. Therefore, we excluded the study from the pooled analysis for hospital LOS. All other studies compared APP-staffed ICUs with physician resident/fellows staffed ICUs and did not show a significant difference for hospital LOS.

Pooled ICU and hospital LOS showed no statistically significant differences for patients that were treated by teams with an ACNP compared with teams without an ACNP. Mean differences were 0.34 days (95% CI, -0.31 to 1.0; $I^2 = 99.85\%$) and 0.02 days (95% CI, -0.85 to 0.89; $I^2 = 90.76\%$), respectively (**Fig. 3**, data on hospital LOS not shown).

APPs in Trauma Service

Three studies reported on the implementation of APPs in trauma services (28, 34, 35), one was a prospective study which integrated two NPs to the trauma service (34). This expedited patient depositions between wards which reduced ICU, hospital, and general ward LOS (18 vs 12 d; 12 vs 9 d; 7 vs 3 d) and thus reduced costs. Two studies were retrospective studies (28, 35). The study of Gillard et al (28) introduced four additional midlevel practitioners to the trauma service and extended their ordinary tasks. This resulted in a significant reduction in urinary tract infection (2.6% vs 0.9%) and reduced ICU LOS (4.08 [sd, 0.27] vs 3.28 [sd, 0.20]). The study of Collins et al (35) implemented five ACNPs

in a special care step-down unit with responsibility for the daily care and communication. The average LOS of the step-down unit decreased 0.35 days (p = 0.0033) in 3 years. The average LOS for the overall trauma service reduced with 0.55 days (p = 0.024) and reduced costs with \$8.9 million in 6 months.

APPs Implemented in Teams

Three studies reported about implementation of PAs and NPs in other teams. Two studies reported about APPs in a critical care outreach team. One of the studies compared the critical care outreach team in two hospitals and introduced a PA in one team. This intervention reduced time to transfer to the ICU significantly with 3.7 hours. ICU and hospital LOS did not change (37). The other study about critical outreach teams introduced an NP as leader of a critical care outreach team (44). The introduction of the NP resulted in a reduction of ICU readmissions of patients which were admitted less than 72 hours without an increase in complications. The study of Kapu et al (42) analyzed the financial impact of NP implementation in a neuroscience ICU team, a cardiovascular ICU team, a surgical ICU team, medical ICU team, and a trauma step-down unit team. After implementation, the gross collections for the neuroscience ICU, surgical ICU, and medical ICU were 62%, 36%, and 47% of the salary and fringe expenses. The team in the cardiovascular ICU exceeded salary and fringe expenses with 32%. The stepdown unit realized 0.8 days adjusted LOS reduction translating in a net charge reduction of \$27.8 million. The risk-adjusted LOS after implementation of NPs decreased for all these units. Scores on satisfaction surveys and protocols were good.

Other

Interventions

Five studies reported on the outcome of technical skills of APPs compared with physician resident/fellows (26, 29–31, 48). The two studies of Alexandrou et al (29, 30) reported complication rates of central venous catheter insertions. Within the ACNP group, the percentage of pneumothorax varied between 0.4% and 1.0% with a catheter-related bloodstream infection rate 0.2–1.3 per 1,000 catheters. This last rate is up to published standards. The retrospective comparative cohort study

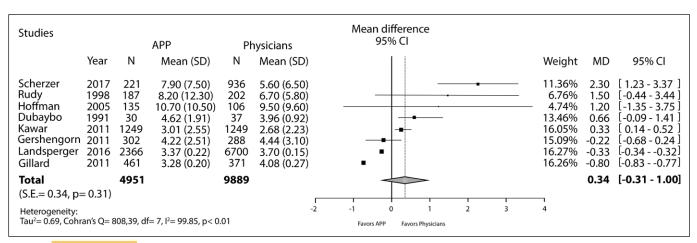


Figure 3. ICU length of stay. APP = advanced practice provider, df = degrees of freedom.

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of Sirleaf et al (48) reported on mortality, hospital LOS, and the ICU LOS after various invasive procedures performed by either ACNPs or physician residents. They found no significant difference within all outcomes while the Acute Physiology and Chronic Health Evaluation III and age was higher in the patients who were treated by the ACNPs (48). The study of Bevis et al (31) was a comparison of complications rates of thoracostomies done by either ACNPs or trauma surgeons. Retrospective analysis showed no significant difference between either groups regarding to complications.

Communication

One study addressed the difference of the quality of handovers done by registered nurses, ACNPs, physician residents, and attending physicians (45). The results of 133 patient handovers demonstrated that the difference in communication depended on the experience level rather than on the clinician type. Furthermore, the physicians engaged more in critique on actions than ACNPs or nurses did. In addition, in an older study by Rudy et al (26), the physician residents discussed patients more actively during rounds and provided more hands-on treatment (p < 0.05), whereas the ACNPs communicated more with the registered nurse (p < 0.05).

Protocol Adherence

There were two studies that reported on protocol adherence. Gracias et al (38) found a higher rate of protocol adherence by ACNPs than by physician residents when measuring prescription of thrombosis prophylaxis (93% vs 98%; p < 0.001), stress-ulcer prophylaxis (51% vs 91%; p < 0.001), and anemia management (67% vs 93%; p < 0.001). Russell et al (46) found less skin breakdown (0% vs 2%; p < 0.05) and less urinary tract infections (2% vs 6%; p < 0.05) in favor of the ACNP.

Patient Satisfaction

One study evaluated the patients' satisfaction rate with the Patient Judgment of Quality Questionnaire group and the functional status of the patients with the Medical Outcome Study Short Form 36. Both the satisfaction rate and the functional performance of patients treated by ACNPs were significantly higher compared with the patients who were treated by physician residents/fellows (47).

Activities

In the study of Hoffman et al (39) the activities performed by either physician residents or PAs were monitored. There was no difference in time spent with the routine management of patients, but the PAs spent more time in coordination of care compared with the physician residents who spent more time on unit activities ranging from meetings to personal time.

Simulation

The study of van Vught et al (50) compared ICU trained PAs in a simulation setting where different scenarios were presented. There was no difference between the performance of physician residents or PAs.

Nonclinical Work

The study of Butler et al (33) investigated optimized billing procedures by PAs on the ICU. After the implementation of PAs, there was an increase in charge capture with net revenue increase of 54%. The results were corrected for the increase in beds during this period.

The study of Jefferson and King (41) measured the impact of an ACNP which discussed the usefulness of the ordered laboratory tests with patients in the ICU. This showed that the total number of laboratory tests increased, but the tests were more specific for the condition of the patient.

DISCUSSION

This review summarizes the current comparable outcome studies concerning the quality of APP care in the ICU/acute care settings when compared with physician resident/fellows care. In general, the literature shows beneficial effects of these practice providers. This review and meta-analysis confirm that good quality of care is provided by APPs in terms of mortality and LOS. The arguments for implementation of APPs are diverse, from providing necessary care in places where no care is available, to improvement of work processes by improving quality or alleviating workload. In addition, continuity of care is often defined as an important benefit. Most studies are, however, descriptive and when comparable outcome studies are available several of these studies are only published as abstract and therefore provided insufficient information to be graded. Several studies with a survey design show the beneficial effects of APPs in acute care (36, 51). Although one of the survey studies was gradable by NOS and reported mortality rates, the survey design made it impossible to technically include the study in the meta-analysis.

All studies that we included were cohort studies. The reason for encountering a cohort design in all the selected studies is probably because this design is the most applicable design instead of, for example, double-blinded randomized controlled trials. Previously, this issue has been addressed by Kleinpell et al (7). Four meta-analyses were constructed from the available studies which showed no significant difference between performance of APPs on the ICU and physician residents/fellows on the ICU suggesting the quality of care of both groups was equal. We only pooled data on the endpoints of mortality and LOS in a meta-analysis because enough relative indisputable data was available on these endpoints. In the limited number of studies on other endpoints, the critical care model incorporating the APP often surpasses the traditional physician resident/ fellow led model in quality of care for critically ill patients. The APP excelled in teams and teamwork. Studies on cost reduction and managing processes effectively by providing continuity of care showed an improvement with APP implementation. In addition, the APP also performed better in protocol adherence, communication, and patient satisfaction. With respect to invasive procedures, only a few studies have been conducted which demonstrated similar outcomes of APPs to physician resident/ fellows. However, additional research is warranted.

A review in a field like this is challenging due to the different study designs. The study of Fry (15) provides a broad overview

and also concluded that research in this field comprises a lot of different study designs. One of the additional conclusions was that practices and job descriptions of APPs differ per country. This might influence the general applicability of the results. Our review for example found only six gradable studies originating from outside the United States (29, 30, 44, 47, 49, 50) and none of these studies matched the inclusion criteria for the meta-analysis.

In studying the available research, we saw a maturation of study designs over the years. The earlier studies used a retrospective design often introducing a few APPs in an existing team instead of comparing teams of APPs to physician residents/fellows. These studies were conducted to establish the impact of APPs by adding them to ICU teams as solution to meeting the workforce needs in the ICU. The results were not always corrected for confounders. Later studies were more often designed for establishing the additional value of the APP over physician residents/fellows in ICU care. The difficulty remains that both APPs and physician residents/fellows work in conjunction with other specialists. The fact that their work is overseen and corrected by physicians makes it difficult to draw a definite conclusion about LOS and mortality. This problem can be approached in two ways. One of the solutions is presented by the study design of Landsperger et al (21). This is a large prospective study where the care during the entire ICU stay was provided by either APPs or physician residents in conjunction with attending physician oversight. When the results were corrected for confounders, the ICU mortality proved lower in the APP group. The difference existed despite the fact that inadequate treatment proposals are corrected by other specialists supervising the physician residents and APPs. Probably, the large prospective study design played a role in measuring this mortality difference.

A second approach to establish an additional value of APPs is to measure specific aspects of care provided by APPs instead of measuring hard endpoints. This has been shown by Sidani et al (47) and Gracias et al (38). They respectively show an improvement in quality of patient care by APPs and an improved adherence to practice guidelines by APPs.

The results of this meta-analysis have to be interpreted with caution. Although this review gives an overall view on the effects of APPs in the critical care setting, with a selection of the evidence-based cohort studies gradable by NOS score, there are differences in design of the studies which are also reflected by the sometimes high heterogeneity in the meta-analysis. In addition, the conversion from medians to means necessary for the comparison may introduce bias by itself as LOS usually shows a skewed distribution. Furthermore, regarding the NOS scale, no structural evaluation of bias was performed. However, of the included NOS studies the minimal score was 5 which implies a reasonable comparability.

Despite these limitations, we have given an overview for both clinicians and researchers of the available literature on APP care in ICU/acute care settings. Those who have to make decisions in their clinical practice can use this review for argumentation. We have shown that the acute care APP seems a promising clinician with regard to quality and, likely, continuity of care. Well-designed comparative cohort studies with larger groups of patients or comparative cohort studies about specific tasks of APPs are needed to further establish their impact.

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