LETTER



Scientific evidence underlying the recommendations of critical care clinical practice guidelines: a lack of high level evidence

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Clinical practice guidelines (CPG) are widely used in critical care medicine (CCM). This study aimed to investigate the distributions of grade of evidence and recommendation in CCM, as well as factors influencing the recommendation classes. We hypothesized that the grade of evidence and publication year were independent determinants of the recommendation classes.

Electronic databases of PubMed and Scopus were searched from inception to March 2017 (details in Supplemental Material 1). CPGs in CCM developed under the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework were included. Data on the following variables were extracted: year of publication, topic of the CPG, recommendation class, and the grade of evidence. Grade levels A, B, C, and D correspond to high, moderate, low, and very low quality of evidence. To examine independent predictors of the recommendation class, a binary logistic regression model was constructed by incorporating variables including year of publication, grade of evidence, and the Appraisal of Guidelines for Research and Evaluation (AGREE) II score [1]. The response variable was the recommendation class, by combing weak and other recommendations into one category. All statistical analyses were performed using R (version 3.3.2). A p value less than 0.05 was considered to be statistically significant.

A total of 88 publications of CPGs involving 3119 recommendations were included for the study (Supplemental Material 2). Only 287 recommendations (9%) were based on grade A evidence. The percentage of grade A evidence ranged from 0% to 30% across topics. There

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were 1698 (54%) strong and 1085 (35%) weak recommendations (Table 1). Although the absolute number of strong recommendations increased over time, the percentage decreased over time [24 (77%), 55 (63%), 216 (69%), 361 (56%), and 349 (52%) in the year 2007, 2008, 2012, 2013, and 2015, respectively]. The logistic regression model showed that publication after 2015 was associated with reduced odds of strong recommendations (odds ratio 0.54; 95% CI 0.46-0.64; p<0.001). As compared with grade A, grade B (OR 0.39; 95% CI 0.26–0.58; p<0.001), C (OR 0.15; 95% CI 0.10-0.21; p<0.001), D (OR 0.13; 95% CI 0.09–0.20; *p* < 0.001), and no evidence (OR 0.09; 95% CI 0.06–0.14; *p* < 0.001) were significantly associated with reduced probability of strong recommendations (Supplemental Material 2), indicating that the quality of evidence is a strong predictor of recommendations [2].

The study showed that a small proportion of CPGs (less than 10%) were based on high level evidence (grade A) in CCM. While the absolute number of strong recommendations increased over time, its percentage decreased over time, probably as a result of the choice of topics where there is less high-quality evidence. Publication year and grade of evidence were independent determinants of strong recommendation. The inverse association between year of publication and strong recommendation might also be explained by guideline panelists having become more rigorous regarding assessment of quality of evidence when issuing recommendations. Our findings were consistent with other specialties. Studies on cardiology showed that the proportion of high level (grade A) evidence was approximately 10% [3, 4]. In oncology, the proportion of recommendations based on high level of evidence was only 6% [5]. Of note, the percentage of high-quality evidence supporting recommendations in

Topics	Grade of evidence ^a										Recommendation class						Total
	A	%	В	%	С	%	D	%	No	%	Strong	%	Weak	%	Other	%	
ACS	0	0	3	5	21	36	20	34	14	24	19	33	25	43	14	24	58
Acute circulatory failure	6	7	26	29	28	31	7	8	24	26	39	43	27	30	25	27	91
Airway	1	2	8	20	29	71	0	0	3	7	32	78	9	22	0	0	41
AKI	11	13	20	23	23	26	7	8	26	30	22	25	39	45	26	30	87
ARDS	1	6	4	22	4	22	5	28	4	22	8	44	8	44	2	11	18
Brain death	6	30	13	65	1	5	0	0	0	0	20	100	0	0	0	0	20
Cardiac arrest	1	0	19	9	63	29	111	51	23	11	54	25	144	66	19	9	217
Cardiac surgery	0	0	4	9	17	36	26	55	0	0	35	74	12	26	0	0	47
Cardiogenic shock	0	0	0	0	3	2	0	0	134	98	113	82	19	14	5	4	137
Corticosteroid insufficiency	0	0	10	100	0	0	0	0	0	0	2	20	8	80	0	0	10
CRRT	0	0	0	0	0	0	52	68	24	32	60	79	16	21	0	0	76
Delirium	35	24	76	52	4	3	30	21	0	0	72	50	49	34	24	17	145
GI	4	9	8	17	18	38	17	36	0	0	27	57	20	43	0	0	47
Hemostatic	0	0	0	0	7	100	0	0	0	0	4	57	3	43	0	0	7
Hyperglycemia	12	22	8	15	17	31	17	31	0	0	22	41	31	57	1	2	54
ICUAW	0	0	0	0	0	0	3	100	0	0	3	100	0	0	0	0	3
Mechanical ventilation	0	0	3	43	3	43	1	14	0	0	1	14	6	86	0	0	7
Neurocrit	37	9	113	28	156	38	62	15	38	9	263	65	143	35	0	0	406
Neuromuscular blocker	0	0	1	4	3	11	7	26	16	59	7	26	10	37	10	37	27
Neutropenic	5	13	2	5	18	46	8	21	6	15	26	67	13	33	0	0	39
Nutrition	1	1	11	7	17	12	44	30	74	50	20	14	66	45	61	41	147
Pancreatitis	18	15	54	45	49	40	0	0	0	0	87	72	34	28	0	0	121
Pneumonia	2	7	15	54	11	39	0	0	0	0	21	75	5	18	2	7	28
Sedation	14	7	96	47	82	40	9	4	3	1	130	64	29	14	45	22	204
Sepsis	49	11	127	29	157	36	70	16	32	7	213	49	190	44	32	7	435
Stress ulcer	0	0	0	0	2	50	0	0	2	50	1	25	1	25	2	50	4
Toxicology	0	0	0	0	4	3	117	97	0	0	81	67	35	29	5	4	121
Tracheostomy	0	0	11	58	4	21	4	21	0	0	11	58	8	42	0	0	19
Transfusion	0	0	11	28	10	25	19	48	0	0	18	45	22	55	0	0	40
Trauma	1	17	0	0	2	33	3	50	0	0	2	33	4	67	0	0	6
Triage	1	2	1	2	11	19	7	12	39	66	2	3	18	31	39	66	59
Ultrasound	62	25	83	34	86	35	0	0	13	5	196	80	25	10	23	9	244
VAP	4	7	12	20	18	31	21	36	4	7	32	54	27	46	0	0	59
Vascular access	16	34	16	34	6	13	0	0	9	19	40	85	7	15	0	0	47
Volume therapy	0	0	2	18	8	73	0	0	1	9	6	55	4	36	1	9	11
VTE	0	0	10	27	22	59	5	14	0	0	9	24	28	76	0	0	37
Total	287	9	767	25	904	29	672	22	489	16	1698	54	1085	35	336	11	3119

Table 1 Distribution of grade of evidence and recommendation class across topics

ACS abdominal compartment syndrome, AKI acute kidney injury, ARDS acute respiratory syndrome, CRRT continuous renal replacement therapy, GI gastrointestinal tract, ICUAW intensive care unit acquired weakness, MV mechanical ventilation, NB neuromuscular blocker, VAP ventilator-associated pneumonia, VTE venous thromboembolism

^a GRADE levels A, B, C, and D correspond to high, moderate, low, and very low quality of evidence

CCM is similar to that in cardiology or oncology, which is in contrast to the higher number of large high-quality trials in those specialties than in CCM. This may be explained by the fact that CCM limits the number of recommendations per guideline compared to cardiology and oncology, so that even with lower numbers of trials, the proportion of recommendations with high level evidence is maintained. In cardiology, a total of 1869 recommendations were issued in 11 guidelines (169.9 recommendations per guideline), compared to 3119 in 88 CCM guidelines (35.4 recommendations per guideline).

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-018-5142-8) contains supplementary material, which is available to authorized users.

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Compliance with ethical standards

Ethical approval

The study did not involve human participants and ethics approval is not applicable.

Conflicts of interest

The authors declare that they have no competing interests.

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