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Title: RELATED FACTORS TO SEMI-RECUMBENT POSITION COMPLIANCE AND PRESSURE ULCERS IN PATIENTS WITH INVASIVE MECHANICAL VENTILATION: AN OBSERVATIONAL STUDY. (CAPCRI STUDY)

Article Type: Research Paper

Keywords: patient positioning; ventilator-associated pneumonia; pressure ulcer; critical care nursing.

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Abstract: Background: Semi-recumbent position is recommended to prevent ventilator-associated pneumonia. Its implementation, however, is below optimal.
Objectives: We aimed to assess real semi-recumbent position compliance and the degree of head-of-bed elevation in Spanish intensive care units, along with factors determining compliance and head-of-bed elevation and their relationship with the development of pressure ulcers. Finally, we investigated the impact that might have the diagnosis of pressure ulcers in the attitude towards head-of-bed elevation.
Methods: We performed a prospective, multicenter, observational study in 6 intensive care units. Inclusion criteria were patients >18 years old and expected to remain under mechanical ventilator for >48 hours. Exclusion criteria were patients with contraindications for semi-recumbent position from admission, mechanical ventilation during the previous 7 days and prehospital intubation. Head-of-bed elevation was measured 3 times/day for a maximum of 28 days using the BOSCH GLM80® device. The variables collected related to patient admission, risk of pressure ulcers and the measurements themselves. Bivariate and multivariate analyses were carried out using multiple binary logistic regression and linear regression as appropriate. Statistical significance was set at $p<0.05$. All analyses were performed with IBM SPSS for Windows Version 20.0.
Results: 276 patients were included (6894 measurements). 45.9% of the measurements were <30.0°. The mean head-of-bed elevation was 30.1 (SD 6.7)° and mean patient compliance was 53.6 (SD 26.1)%. The main reasons for non-compliance according to the staff nurses were those related to the patient's care followed by clinical reasons.
The factors independently related to semi-recumbent position compliance were intensive care unit, ventilation mode, nurse belonging to the research team, intracranial pressure catheter, beds with head-of-bed

elevation device, type of pathology, lateral position, renal replacement therapy, nursing shift, open abdomen, abdominal vacuum therapy and agitation. Twenty-five patients (9.1%) developed a total of 34 pressure ulcers. The diagnosis of pressure ulcers did not affect the head-of-bed elevation. In the multivariate analysis, head-of-bed elevation was not identified as an independent risk factor for pressure ulcers. Conclusions: Semi-recumbent position compliance is below optimal despite the fact that it seems achievable most of the time. Factors that affect semi-recumbent position include the particular intensive care unit, abdominal conditions, renal replacement therapy, agitation and bed type. Head-of-bed elevation was not related to the risk of pressure ulcers. Efforts should be made to clarify semi-recumbent position contraindications and further analysis of its safety profile should be carried out.

Response to Reviewers: First of all, we would like to thank all the comments provided to improve the manuscript. All modifications made in the manuscript are highlighted in yellow.
We will response point by point to all questions asked:
Initial comments:

* All full papers must have an abstract. For research and review papers this must be structured
The manuscript already has an structured abstract (background, objectives, methods, results and conclusions)

* For research and review papers, the title should be in the format 'Topic / question: design/type of paper'
The title of the manuscript already follows the recommendation as can be seen: “Related factors to semi-recumbent position compliance and pressure ulcers in patients with invasive mechanical ventilation: an observational study. (CAPCRI study)”

* Research and review must include short bullet points for 'what is already known and 'what this paper adds' (up to 3 bullets for each)
The sections of “what is already known and what this paper adds” has been structured in bullet points.

* All full papers must be accompanied by a completed author checklist, available to download in the Guide for Authors (http://cdn.elsevier.com/promis_misc/IJNSchecklist2.doc) - please upload the word document as a separate file
The checklist has been updated and uploaded.

* All research and review papers must be checked against the relevant reporting guidelines
The checklist has been updated and uploaded.

* The journal strongly discourages the use of abbreviations (including acronyms and initials). Use only abbreviations that are universally used and only when absolutely necessary.
The abbreviations have been reviewed and reduced.

Finally we ask that you closely proof read and check the use of English in the manuscript. This makes it far easier for reviewers to make clear recommendations based upon the scientific merit of your paper and avoids requests for further revision if the science is acceptable.

The manuscript has been proof read and checked the English.

Reviewer comments:

COMMENT FROM ASSOCIATE EDITOR: Thank you very much for submitting your work to the IJNS. In addition to the reviewer comments please pay careful attention to the author instructions.
- Please use abbreviations sparingly and avoid acronyms as much as possible (e.g. MAP, IAP etc). Please also check the tables (e.g. what is a T-piece, sat/FiO2 etc.). While many readers will know these abbreviations, many will not.
The number of abbreviations has been reduced. The following abbreviations have been deleted: VAP, BMI, MAP, IAP. In the new version, only the most frequent abbreviations appear on the text: ICU, SP, HOBE, MV.
However, in tables, the abbreviations are still present due to the available space but on the legend are defined all the abbreviations used. Acronyms like Sat/FiO2 and APACHE II have been defined in table legends as well as T-piece has been explained.
- You structured your manuscript according STROBE. Please indicate the page numbers where you addressed the items instead of using crosses. Please expand the item #8. Please clearly describe ALL instruments used, e.g. APACHE later appearing in the table. Please also address items #9 and #15.

The item 8 has been described deeply in methods section and accompanied by more information in supplementary data because we thought it would be easier for the reader.
The item 9 has been included in the methods section.
We believe that the item 15 is already included in all the results section. More importantly, in pages 9-10 for semirecumbent position outcomes and 15 for pressure ulcers outcomes.

Reviewer #1:
The authors performed a prospective multicentre cohort study to assess adherence with the semi-recumbent positioning recommendation and the relationship with pressure ulcers. I have the following comments...
1) Abstract: the abstract states... "The diagnosis of PUs did not affect the head-of-bed elevation." But according to the objectives of the study it is the other way around: "Head-of-bed elevation was not associated with risk of PU development" (unless the investigators want to report whether nurses considered the existence of PUs in their decision to perform HoB elevation).
The analysis of the relationship between pressure ulcers and head-of-bed-elevation intended to find out if the head-of-bed elevation had any impact on the risk of PU. However, on the other hand, we analysed the impact of the diagnosis of a PU to the head-of-bed elevation to know if the attitude from nurses changed. We acknowledge that this could be confusing when analyzing the conclusions from the abstract and objectives. We added this objective in the abstract and in the manuscript.

2) Background - 1st paragraph: From what the authors write it is clear that exists at least some controversy about the issue of semirecumbent positioning (for whaztever reson, either effectiveness to reduce VAP risk

or in terms of feasibility); for that reason a reference focused on the controversial aspects of VAP prevention would be better placed here (e.g. Lorente L, et al. Am J Respir Crit Care Med 2010).
The reference has been added.

3) Please clarify: the inclusion criterion "requiring >48 hrs of MV"... was this an anticipated estimate that the patient probably needed >2 days of MV or were patients only included when they were already for 2 days on the ventilator?
A clarification has been included in the Methods section regarding this point:
To ensure the collection of the HOBE from the first 24h of MV, patients were included as soon as possible and if they were under MV less than 48 hours were excluded.
4) What is meant by "the complexity of the centers"?
This sentence has been changed to avoid confusion. The new version is:
The level of care of the centers were 2a and 2b corresponding to high or moderate complexity of care.
The assignation of the centers is made by the Catalan Government and it is referenced in the text. The document is made for the assistance of politraumatic patients but is applicable to all patients because they describe the requirements of the centers to belong to the different levels of care.
5) What is meant by "collection rate, 86,3%"? Does this mean that 13,7% of presumed HoBe evaluations were not performed? If so, is this corrected for the fact that when patients are extubated after 1 measurement it is normal that the two other (for that day) are not needed.
The collection rate means the measurements obtained from all possible measurements (considering all measurements where the patient was with MV and was in the ICU on the bed). If the patient was extubated, the following measurements were not performed per protocol.
This has been clarified on the Methods section of the manuscript: HOBE was determined 3 times per day (one time per nursing shift) while the patient was under MV or T-piece for weaning evaluation and present in the ICU lying on the bed.
6)Table 1 : the ** part of the table: do the n (%) represent the number and % of the HOBE measurements?
Yes, the measurements with those nurses characteristics.
7) IMPORTANT: the authors reported failure to adhere with the HOBE recommendation when this was <30°. However, the trial by Van Niewenhove et al. demonstrated that there was no difference in VAP when a group with about 11° (assumed to be 30°) was compared with 28° (assumed to be 45°). Therefore I would like to know the % of patients/measurements in which the HOBE was <10° because this is probably the critical threshold.
There were only 10 (0.14%) measurements <10° from all 6894 observations. The minimum HOBE was 4.0° and the maximum of this group was 10.0°. The mean elevation within this group was 8.7° (SD 1.97°).
8) Table 3: do I miss the only strong factor related with SP compliance (ICU)?
Thanks for this really important comment. This was missing and it has been included. Thank a lot for discovering this relevant mistake.
9) Vascular access and PS compliance: there is no meaningful rational between subclavian/jugular access and lower HOBE; the only factor that might have been related is femoral access as it might have lead to occlusion.
We acknowledge that this is a limitation of the study as it is discussed in page 20 of the manuscript. We could not conclude anything else due to the small sample of femoral access. On the other hand, other factors

might play a role because many times in clinical practice jugular access has complications with renal replacement therapy due to anatomical issues. However, all the potential factors influencing this relationship are out of our control.
10) In reporting on multivariate analysis in the text do mention as well in which direction the variable is associated with increasing SP (e.g. ventilation mode: the higher the patients' independcy the higher the SP compliance). This will make the paper more easily to read/understand.
The text has been clarified in different parts of the results sections. Changes are highlighted in yellow.
11) Table 4a: which ICU did you take as reference category? The one with the largest sample?
The ICU taken as reference is ICU 1. This was chosen because it was the one with the lowest HOBE and SP compliance and it was easier to show the results.
12) Table 5: I assume that "No UPP" means "No pressure ulcer"...?
Yes. Thanks for the appreciation, this was a translation oversight.
13) Table 6 and related text in the Results: please confirm it are HIGH concentrations of albumin and pre albumine that are related with the incidence of PUs (and not vice versa). Also when were (pre) albumine levels recorded? On admission only, for example...?
In the related text it is stated that albumin and pre-albumin are shown to be preventive factors for PU. And in table 6, in the legend it states OR >1 is a risk factor for PU. And Albumin and Pre-albumin have OR <1. Therefore, having higher values of albumin and pre-albumin are preventive factors for PU development. On the other hand, the values recorded are the ones prior to PU diagnosis. We recorded weekly values and the values included in the model are the last available before the diagnosis.
14) Discussion: page 18, line 11: omit the word "massive"
Word deleted.
15) Discussion: page 19, line 18-20: Rephrase: "...% of patients developed PUs in this study (n=25) and this is the highest proportion of reported in studies assessing the association between HOBE and PU risk."
This sentence has been rephrased according to your recommendation.
Reviewer #2: Many thanks for this well written article, it is clearly presented and easy to read and understand. The one comment I have relates to the sample size calculation, this has been undertaken with regard to SP, not with regard to the development of pressure ulcers. Thus,the regression may be under-powered for inference pertaining to pressure ulcers, given the requirement for 10 incidences of pressure ulcer per variable. The regression includes 12 variables, thus 120 pressure ulcer incidences would be needed, using the rule of ten (Mallett S, Royston P, Dutton S, Waters R, Altman DG. Reporting methods in studies developing prognostic models in cancer: a review. BMC Med 2010;8:20). This point needs to be addressed within the paper.
Thanks for this relevant consideration. This aspect has been addressed in the limitations sections:
Third, the sample size calculation was performed for the main objective of the study and there was no sample calculation for the analysis of PU due to the unknown prevalence in the participating centers. Therefore, the multivariate analysis performed with regards to the relationship between HOBE and PU might be underpowered according to Mallet S, et al. [45]. Thus, a bigger sample should be recruited to confirm or refuse the results obtained in our analysis.

AUTHOR COMMENTS:
- We included in table 4b the information from the Bed with HOBE device which was missing by mistake.

May 1st, 2016

Ian Norman, PhD, RN, BABCP, FRNC, FEANS, FAAN
Editor-in-Chief
International Journal of Nursing Studies
Florence Nightingale Faculty of Nursing and Midwifery
London, United Kingdom

Dear Prof Norman,

It is with pleasure to send you back the new version of the manuscript entitled: *"Related factors to semi-recumbent position compliance and pressure ulcers in patients with mechanical ventilation: an observational study. (CAPCRI Study)"*
We have addressed all the comments made by the reviewers and by the associated editor.

We hope that the new version fulfills the requirements of the journal and the reviewers.

In case any other clarification or modification is required we will be delighted to overcome it.

Thanks for considering the manuscript for publication in International Journal of Nursing Studies.

Yours sincerely,

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RELATED FACTORS TO SEMI-RECUMBENT POSITION COMPLIANCE AND PRESSURE ULCERS IN PATIENTS WITH INVASIVE MECHANICAL VENTILATION: AN OBSERVATIONAL STUDY. (CAPCRI STUDY)

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Conflicts of interest: none

Autors' contributions

MLS has designed the study and drafting the manuscript. MLS, RGB, ALC, APT, NCD, MPG, CPE have participated in the acquisition of data. MLS and JFB have made the analysis and interpretation of data. MU interpreted the data and reviewed critically the manuscript. MFJ and AS have supervised the correct performance of the study and reviewed critically the manuscript. All authors have revised the manuscript critically and approved the final version of manuscript for publication.

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Isabel Blanco-Sánchez, Laura Palomino-González, Marta Domenech-Aguilera, Remei González-Engroba, Rosa M. Pérez-Martín, Cristina Alfonso-Arias, Concha Alvárez-Martínez, Cesar Vargas-López (Quiron Salud-Hospital General de Catalunya, Barcelona, Spain)

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Funding

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The funding organisms had no role in the study design, data collection, analysis interpretation, manuscript drafting or in the decision to submit the manuscript for publication. Funding financed the devices for head-of-bed elevation measurement (BOSCH GLM80®) and diffusion of the results by assisting to scientific meetings.

*Contribution of the paper

WHAT IS ALREADY KNOWN ABOUT THE TOPIC:

- Semi-recumbent position is a widely recommended measure to prevent ventilator-associated pneumonia in critically ill patients with mechanical ventilation. However, on one hand, it is known that its implementation is below optimal and on the other hand, there is only one randomized clinical trial that demonstrated a preventive effect of this position for ventilator-associated pneumonia.
- Some studies have evidenced some factors that affect its compliance. Moreover, until 2014 there was a conflict between guidelines for the prevention of ventilator-associated pneumonia which included the head-of-bed elevation at 30-45º and the guidelines for the prevention of pressure ulcers which recommended the head-of-bed elevation below 30º. However, this confrontation has been solved since 2014.

WHAT THIS PAPER ADDS:

- Worldwide, this is the third multicenter study published which addressed this topic. Besides, is the one with the largest follow-up of the head-of-bed elevation and with the biggest sample for the evaluation of the relationship between pressure ulcers and semi-recumbent position.
- It is the first to address this issue from two different perspectives: from an objective point of view through observations and from a subjective point of view through investigating the reasons why nurses do not apply the recommendation.
- This study identified risk factors for the development of pressure ulcers which consolidate the body of knowledge.

***Author Checklist**

IJNS AUTHOR CHECKLIST ***Authors of all papers should submit this checklist plus the checklist from the relevant reporting guideline together with their manuscript.*** *Part 1* identifies basic requirements for the manuscript submission *(mandatory for all submissions)*

Part 2 identifies recognized guidelines for scientific reporting, which you should use to prepare your manuscript *(required for systematic reviews and original research)*

PART 1 Basic requirements	***Author response or further detail – please complete the boxes below***
Word count	Abstract: 390 words. Manuscript: 3569 words
Was ethical approval given and by whom? (give any reference number)	Yes. The study was approved by the 6 ethics committees from the 6 intensive care units that participated. There is no reference number from any committee. It was referred as the protocol name: CAPCRI Study
Please state any conflicts of interest	None
Please state sources of funding and the role of funders in the conduct of the research	The project was awarded with the following prices: 14º National Award of nursing research. Hospital Universitario Marqués de Valdecilla (2012), Award to the best oral communication of nursing in XXXI Jornades Catalanes d'infermeria Intensiva I Crítica (2014) and 2º Award to the best research study from the Col.legi Oficial d'Infermeres i Infermers de Tarragona (2015). The funding organisms had no role in the study design, data collection, analysis interpretation, manuscript drafting or in the decision to submit the manuscript for publication. Funding financed the devices for head-of-bed elevation measurement (BOSCH GLM80®) and diffusion of the results by assisting to scientific meetings.
Please state any study registry number (e.g. ISRCTN)	None

For the items below, please tick in the right hand column to confirm you have included/addressed the items:		**Tick**
Title	Confirm that the title is in the format 'Topic / question: design/type of paper' and identifies the population / care setting studied. *(e.g. The effectiveness of telephone support for adolescents with insulin dependent diabetes: controlled before and after study).* The structure is optional for discussion papers, editorials and letters)	x
Abstract	A structured abstract appropriate to the design of the study is included (see *guidelines for authors)*.	x
	No references are cited in the abstract.	x
Key words	Between four and ten key words have been provided in alphabetical order, which accurately identify the paper's subject, purpose, method and focus. Use the Medical Subject Headings (MeSH®) thesaurus or Cumulative Index to Nursing and Allied Health (CINAHL) headings where possible (see http://www.nlm.nih.gov/mesh/meshhome.html).	x
Highlights	Bullet points have been included that identify existing research knowledge relating to the specific research question / topic (what is already known about the topic?) and a summary of the new knowledge added by this study (what this paper adds) *(see Guide for Authors*, does not apply to editorials or letters)	x
Abbreviations	No abbreviations are used in the title / abstract. Use of abbreviations /acronyms in the paper is minimised and restricted to those that are likely to be universally recognized (e.g. USA)	x
References	All citations in the paper have a complete and accurate reference in the reference list (see *Guide for Authors)*	x
Other Published accounts	*All* published and in press accounts of the study from which data in this paper originate are referred to in the paper and the relationship between this and other publications from the same study is made clear (see *Guide for Authors*) (Please upload copies of all previous, current and under review publications from this study and / or give full details below)	x

	Please provide references of ANY other papers using data from the study that this paper is based on) below. - Llauradó-Serra M, Güell-Baró R, Lobo-Cívico A, Castanera-Duro A, Pi-Guerrero M, Piñol-Tena A, et al. Factors associated with compliance to the semi-recumbent position in the patient on mechanical ventilation: CAPCRI-Q questionnaire. Enferm Intensiva. 2015;26(4):123–36.	
	The study is referred to by a distinctive name which will be used in any future publications to identify that it is the same study (e.g. RN4Cast)	x
Authorship	All authors and contributors sufficiently acknowledged as per Guide for Authors.	x

PART 2 Standards of reporting	The editors require that manuscripts adhere to recognized reporting guidelines relevant to the research design used. These identify matters that should be addressed in your paper. Authors of research papers and systematic reviews are required to submit a checklist relevant to the research design they have used. The checklist will be drawn on within the peer review process. Please indicate which guideline (below) that you have referred to and ensure that the relevant checklist is uploaded. These are not quality assessment frameworks and your study need not meet all the criteria implied in the reporting guideline to be worthy of publication in the IJNS. The checklists do, however, identify essential matters that should be considered and reported upon. For example, a controlled trial may or may not be blinded but it is important that the paper identifies whether or not participants, clinicians, outcome assessors and analysts were aware of treatment assignments. *Reporting guidelines endorsed by the IJNS are listed below:*	**Checklist submitted****
Observational cohort, case control and cross sectional studies	STROBE **St**rengthening the **R**eporting of **Ob**servational Studies in **E**pidemiology http://www.equator-network.org/index.aspx?o=1032	x
Quasi experimental / non-randomized evaluations	TREND - Transparent Reporting of Evaluations with Non-randomized Designs http://www.cdc.gov/trendstatement/	
Randomised (and quasi-randomised) controlled trial	CONSORT – Consolidated Standards of Reporting Trials http://www.equator-network.org/index.aspx?o=1032	
Study of Diagnostic accuracy / assessment scale	STARD Standards for the Reporting of Diagnostic Accuracy studies http://www.equator-network.org/index.aspx?o=1032	
Systematic Review of Controlled Trials	PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses http://www.equator-network.org/index.aspx?o=1032	
Systematic Review of Observational Studies	MOOSE Meta-analysis of Observational Studies in Epidemiology http://www.equator-network.org/index.aspx?o=1032	
Qualitative studies	COREQ: Consolidated criteria for reporting qualitative research Tong, A., Sainsbury, P., Craig, J., 2007. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care* 19 (6), 349-357. (http://dx.doi.org/10.1093/intqhc/mzm042)	
Other (please give source)		

Not applicable (please elaborate)		

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4,5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7 suplementary data*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8

(*c*) Explain how missing data were addressed	7-8
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	8-9
		(c) Consider use of a flow diagram	8-9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-10. supl material
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*9-10,15*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-17
		(*b*) Report category boundaries when continuous variables were categorized	10-17
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-17
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21-22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-22
Generalisability	21	Discuss the generalisability (external validity) of the study results	21-22
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

RELATED FACTORS TO SEMI-RECUMBENT POSITION COMPLIANCE AND PRESSURE ULCERS IN PATIENTS WITH INVASIVE MECHANICAL VENTILATION: AN OBSERVATIONAL STUDY. (CAPCRI STUDY)

ABSTRACT

Background: Semi-recumbent position is recommended to prevent ventilator-associated pneumonia. Its implementation, however, is below optimal.

Objectives: We aimed to assess real semi-recumbent position compliance and the degree of head-of-bed elevation in Spanish intensive care units, along with factors determining compliance and head-of-bed elevation and their relationship with the development of pressure ulcers. Finally, we investigated the impact that might have the diagnosis of pressure ulcers in the attitude towards head-of-bed elevation.

Methods: We performed a prospective, multicenter, observational study in 6 intensive care units. Inclusion criteria were patients ≥18 years old and expected to remain under mechanical ventilator for ≥48 hours. Exclusion criteria were patients with contraindications for semi-recumbent position from admission, mechanical ventilation during the previous 7 days and prehospital intubation. Head-of-bed elevation was measured 3 times/day for a maximum of 28 days using the BOSCH GLM80® device. The variables collected related to patient admission, risk of pressure ulcers and the measurements themselves. Bivariate and multivariate analyses were carried out using multiple binary logistic regression and linear regression as appropriate. Statistical significance was set at $p<0.05$. All analyses were performed with IBM SPSS for Windows Version 20.0.

Results: 276 patients were included (6894 measurements). 45.9% of the measurements were <30.0º. The mean head-of-bed elevation was 30.1 (SD 6.7)º and mean patient compliance was 53.6 (SD 26.1)%. The main reasons for non-compliance according to the staff nurses were those related to the patient's care followed by clinical reasons.

The factors independently related to semi-recumbent position compliance were intensive care unit, ventilation mode, nurse belonging to the research team, intracranial pressure catheter, beds with head-of-bed elevation device, type of pathology, lateral position, renal replacement therapy, nursing shift, open abdomen, abdominal vacuum therapy and agitation. Twenty-five patients (9.1%) developed a total of 34 pressure ulcers. The diagnosis of pressure ulcers did not affect the head-of-bed elevation. In the multivariate analysis, head-of-bed elevation was not identified as an independent risk factor for pressure ulcers.

Conclusions: Semi-recumbent position compliance is below optimal despite the fact that it seems achievable most of the time. Factors that affect semi-recumbent position include the particular intensive care unit, abdominal conditions, renal replacement therapy, agitation and bed type. Head-of-bed elevation was not related to the risk of pressure ulcers. Efforts should be made to clarify semi-recumbent position contraindications and further analysis of its safety profile should be carried out.

KEY WORDS: patient positioning; ventilator-associated pneumonia; pressure ulcer; critical care nursing.

BACKGROUND

Semi-recumbent positioning (SP) is defined as head-of-bed elevation (HOBE) ≥30º and is highly recommended in the international guidelines [1–4] for the prevention of ventilator-associated pneumonia. However, despite the fact that its use is broadly recommended, evidence supporting its role is limited [5,6]. So far there have been few clinical trials demonstrating a reduction of broncoaspiration at 45º compared to 0º [7–9] and just one randomized clinical trial that demonstrated that the position at 45º compared to 0º prevented ventilator-associated pneumonia [10].

Studies focusing particularly on SP compliance have found that the mean HOBE ranges from 19.2º to 28º [11–13] and that this is below the optimal value, which is between 22.3% and 40.9% [13–16].

Many strategies aiming to increase SP compliance have been described, such as training sessions [14,17], devices to remind staff of the importance of SP [18] and even considering SP as a clinical monitoring parameter [19,20]. However, maintaining patients positioned at ≥30º still appears to be challenging.

One of the potential adverse effects of SP is the risk of pressure ulcers (PUs), which has been one of the main concerns when complying with the recommendation [21]. Current guidelines for PU prevention from the National Pressure Ulcer Advisory Panel prioritize the prevention of ventilator-associated pneumonia over PUs [22].

In addition, critically ill patients are very heterogeneous and there are multiple factors that could hinder compliance with the SP recommendation as described previously [13].

The aim of the present study was to assess real SP compliance and the degree of HOBE in Spanish intensive care units (ICUs), along with related factors to the degree of HOBE and SP compliance and their relationship with the development of PUs and the impact that the PU diagnosis might have in the attitude towards HOBE.

METHODS

Design and subjects

This was an observational, prospective, multicenter study conducted in 6 Spanish ICUs from March to December 2013. The study was approved by the Ethics Committees of each center, and the written informed consent of the patient or a family member was required in one ICU (references are listed in the 'Ethics approval and consent to participate' section).

All patients who met the following criteria were included: patients ≥18 years old expecting to require ≥48 hours of mechanical ventilation (MV) and HOBE determination within the first 24 hours of MV. Exclusion criteria were SP contraindications from admission (suspected or confirmed spinal cord injury, pelvic fracture, reverse trendelenburg or prone position), non-invasive MV, MV during the last 7 days or intubation in a prehospital setting.

To ensure the collection of the HOBE from the first 24h of MV, patients were included as soon as possible and if they were under MV less than 48 hours were excluded.

ICU characteristics

All centers were teaching hospitals: three public, one private and two private with contracts with the public healthcare system. The level of care of the centers were 2a and 2b corresponding to high or moderate complexity of care [23]. The participating ICUs had between 8 and 18 beds. The nurse patient/ratio was similar within ICUs, with the vast majority being 1 nurse to 2 patients. All ICUs were enrolled in the national "Neumonía Zero" project, which includes avoidance of HOBE at 0º and when possible >30º [24].

Calculation of sample size

A study performed in the coordinating center was used as the reference for calculating sample size [25]. Expecting a SP compliance of 25% and assuming an error margin of 4% and a confidence level of 95%, 431 measurements were needed to evaluate SP compliance. Considering the epidemiological data available from the participating ICUs, this meant that 29 patients per center needed to be included. However, due to the unknown prevalence of the factors to be evaluated, the sample size was set at 50 patients per ICU, representing 300 patients in total.

Study procedure

HOBE was measured during 28 consecutive days of ICU admission or until the patient was disconnected from the MV, discharged from the ICU or died.

HOBE was determined 3 times per day (one time per nursing shift) while the patient was under MV or T-piece oxygenation mode for weaning evaluation and present in the ICU lying on the bed. All measures were performed using the same

device (BOSCH GLM80®) and the same procedure (Figure 1-supplementary data). The device was calibrated from the factory and was only used for this trial.

If the observed HOBE was seen to be <30.0º, the researcher asked the nurse responsible for the patient what the underlying reason was. All staff members were aware of the study so as to avoid the perception that it was of a punitive nature.

Variables and definitions

The variables recorded included demographic and clinical data relating to patient admission, PU development and the risk factors and variables relating to each measurement of the HOBE. These included variables related to the staff nurse and each patient's characteristics and condition.

Semi-recumbent compliance in each observation was defined as HOBE ≥30.0º. Any measurement below 30º was considered non-compliance. The only measurements considered valid were those obtained with the BOSCH GLM80®, regardless of whether the bed had its own system.

Pressure ulcers were defined in accordance with the European Pressure Ulcer Advisory Panel / National Pressure Ulcer Advisory Panel [26].

There were differences between centers as regards the scales used for PU risk evaluation (EMINA [27], BRADEN [28], NOVA-4 [29]) and sedation evaluation (RASS [30] and RAMSAY [31]) due to the observational nature of the study. In both cases data were categorized to enable a global analysis. PU risk evaluation was categorized as high risk (EMINA and NOVA-4 ≥8 points, BRADEN ≤12 points), moderate risk (EMINA and NOVA-4 4-7 points, BRADEN 13-14 points) or low risk

(EMINA and NOVA-4 1-3 points, BRADEN ≥15 points) [32]. Sedation was stratified as no sedation (RASS 0 points, RAMSAY 1-3 points), moderate sedation (RASS -3 to -1 points, RAMSAY 3 points) or deep sedation (RASS -5 and -4 points, RAMSAY 4-6 points). A more detailed information of the variables evaluated is presented in the Supplementary data.

Potential source of bias

The potential bias of the results arises from the need of multiple investigators. In order to minimize it, all investigators were trained by the principal investigator of the study and a responsible was designated to all centers to provide immediate feedback in case of need.

Ethical approval

Data records were codified to maintain the confidentiality. Good research practice guidelines and current laws regarding data protection (LOPD 15/1999) were followed during the study. The project was evaluated and approved by the ethics committees from all participating centers. In one centers informed consent from patient or legal representative was obtained due to committee' requirement.

Statistical analysis

Only patients with a data collection ≥60.0% of the possible measurements were included in the analysis. The analyses were performed considering the individual observations as units of study. In cases where the unit of study was the patient instead of the individual observation, this is specified in the text.

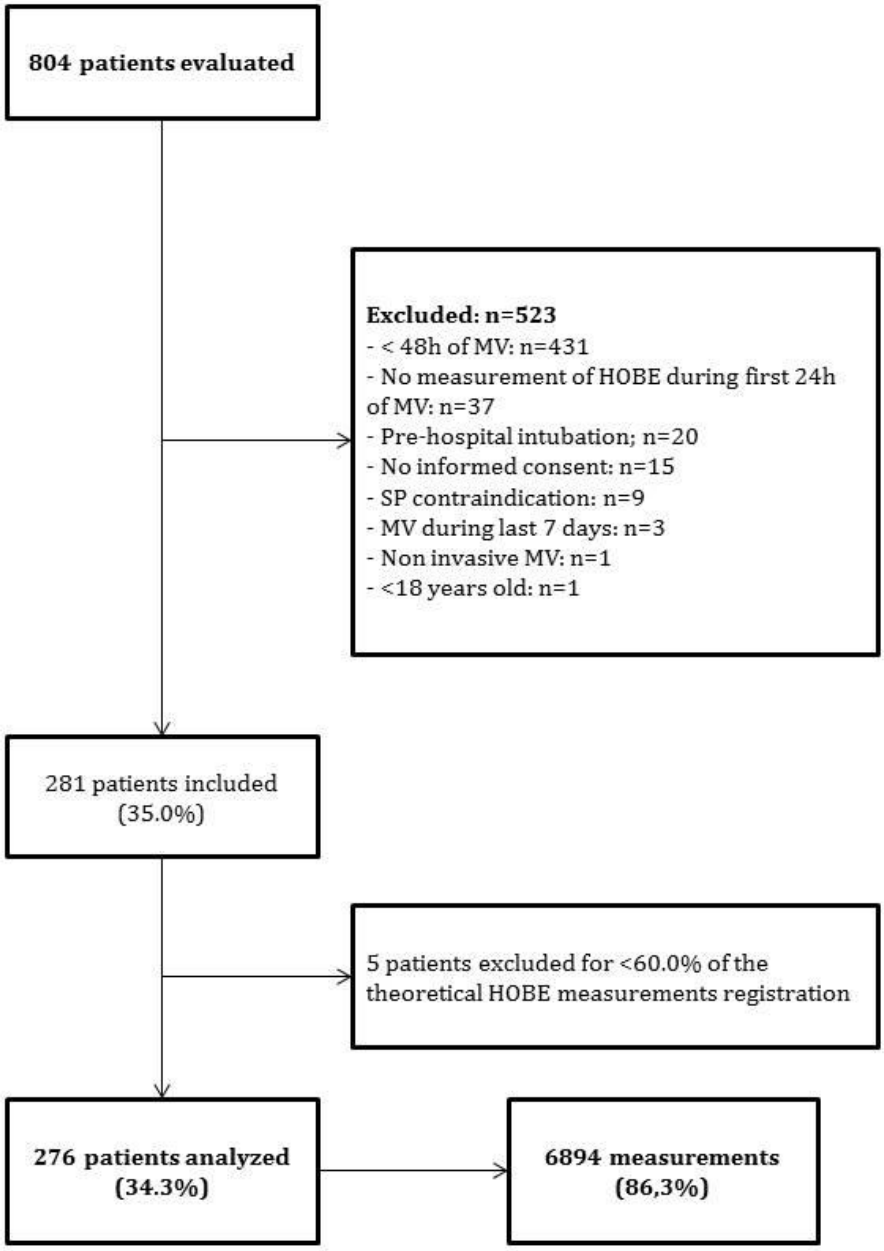
Descriptive data were expressed as mean and standard deviation (SD), median and percentile 25 and 75 (P_{25}-P_{75}) or frequencies (n) and proportions (%), as appropriate. The reasons for non-compliance according to staff nurses were analyzed in terms of categories and sub-categories as per their similarities.

Bivariate analysis was conducted using a Student's t-test for independent samples, ANOVA, the Mann-Whitney U test, the Wilcoxon test or a chi-square test, as appropriate. The Bonferroni correction was used in all multiple comparison analyses and the p value provided corresponds to the adjusted value. Due to the high number of measurements recorded, the strength of association was calculated [33]. Statistical significance was considered when $p<0.05$ for all analyses. The variables included in the multivariate analysis had a corrected p value of <0.05 in the bivariate analysis or were clinically relevant. Multivariate binary logistic regression analysis or multiple linear regression analysis were used with the introduce method. In the analysis to evaluate the relationship between HOBE and PU development, weighting was used due to the improvement of the statistical model. All analyses were performed using IBM SPSS Version 20.0 for Windows®.

RESULTS

Of the 804 patients evaluated, 276 were enrolled, obtaining a total of 6894 observations (86.3% collection rate) (Figure 2).

Figure 1. Flow diagram of the patients analyzed in the study.



All ICUs included around 50 patients, except for one that had only 31. The median number of observations obtained per patient was 18 (P_{25}-P_{75} 9-34) during a mean

of 10.6 (SD 7.5) study days. Table 1 shows the patients' and nurses' characteristics and comparisons between ICUs.

One hundred ninety-five patients (70.7%) were males with a mean age of 63.5 (SD 14.5) years old and an APACHE II score of 18.5 (SD 7.2) points. Patients were admitted mainly due to a medical diagnosis (57.2%) and had a mean ICU length of stay of 20.0 (SD 22.3) days. 27.5% of them died. There were no differences between patient characteristics in different ICUs apart from the mean APACHE II score and the admission diagnosis ($p<0.05$). The characteristics of the nurses also varied depending on the ICU, with statistically different aspects being intensive care experience, critical care training and patients cared for by a researcher nurse ($p<0.05$). Mean SP compliance per patient during the study period was 53.2% (SD 23.8%). 17% of the patients had a compliance rate below 25%, while 23.9% had a compliance rate of between 75-100%. Overall, 35.5% of the patients had a compliance rate of between 50-74.9%. The reasons for the study ending were as follows: MV disconnection (n=156; 56.5%), death (n=56; 20.3%), ICU discharge (n=38; 13.8%) and completion of the study (n=26; 9.4%).

Semi-recumbent position compliance and head-of-bed elevation

Head-of-bed elevation ranged from 4º to 63.5º. Half of the observations were between 26.4º and 33.6º. The mean HOBE was 30.1 (SD 6.7)º and 3164 (45.9%) observations were below 30.0º.

The SP compliance and HOBE rates differed significantly between ICUs, apart from HOBE in two comparisons (ICU3 vs ICU6 and ICU4 vs ICU5) (Table 1-supplementary data).

Reasons for non-compliance according to staff nurses

Of all the measurements below 30.0º (n=3164) observed, 2146 reasons for non-compliance were obtained from staff nurses, with two reasons being reported on 92 occasions (67.8% collection rate). The main reasons concerned patient care (n=1484; 66.3%), clinical causes (n=742; 33.2%) and obstacles related to resources (n=12; 0.5%) (Table 2).

Table 2. Reasons for non-compliance according to staff nurses

	N (%)
1. PATIENT'S CARE	**1484 (66.3)**
1.1. PATIENT'S CARE RELATED TO THE NURSE CRITERIA	1287 (86.7)
1.1.1.Visual perception (they believed it was correct)	568 (44.1)
1.1.2.The bed device to measure HOBE indicated 30º	460 (35.7)
1.1.3.Patient's comfort as per nurse opinion	132 (10.3)
1.1.4.No reason / mistake	122 (9.5)
1.1.5. Life support therapy limitation due to end-of-life	4 (0.3)
1.1.6.Someone has lowered it	1 (0.1)
1.2. PATIENT'S CARE DUE TO PHYSICAL REASONS	197 (13.3)
1.2.1.Lateral position	75 (38.1)
1.2.2.Procedures	47 (23.9)
1.2.3.Patient's wish	44 (22.3)
1.2.4.Patient's does not accept it	16 (8.1)
1.2.5.Sliding of the patient in the bed	10 (5.1)
1.2.6.Pressure ulcer or injury in sacrum / risk of pressure ulcer	3 (1.5)
1.2.7.Obesity / anasarca	2 (1.0)
2. PATIENT'S CLINICAL CONDITIONS	**742 (33.2)**
2.1. INGUINAL	186 (25.1)
2.1.1.Femoral renal replacement catheter / high pressures in the therapy due to the femoral catheter	165 (88.7)
2.1.2.Inguinal devices	17 (9.1)
2.1.3.Inguinal gangrene	4 (2.2)
2.2. ABDOMINAL	166 (22.4)
2.2.1.Abdominal vacuum therapy / open abdomen	86 (51.8)
2.2.2.Abdominal surgery	39 (23.5)
2.2.3.Abdominal distension	36 (21.7)
2.2.4. Abdominal lavages/ devices/ drainages/ gastrostomy	3 (1.8)
2.2.5.Hematochezia / diarrhea	2 (1.2)
2.3. HEMODYNAMICS	150 (20.2)
2.3.1.Hemodynamic instability	146 (97.3)
2.3.2.Pacemaker/ intra-aortic balloon pump/ Sengestaken tube	4 (2.7)
2.4. NEUROLOGIC	134 (18.1)
2.4.1.Agitation/ self-extubation risk/ uneasy patient	124 (92.5)
2.4.2.Ventricular drainage	8 (6.0)
2.4.3.Convulsions	1 (0.7)
2.4.4.Cervical/ neck/ cranial drainage	1 (0.7)

2.5. RENAL	84 (11.3)
2.5.1.Renal replacement	68 (81.0)
2.5.2.Renal replacement catheter (except for the femoral)	16 (19.0)
2.6. RESPIRATORY	21 (2.8)
2.6.1.Recent tracheostomy/ post-surgery	13 (61.9)
2.6.2.Respiratory instability	8 (38.1)
2.7. LOWER EXTREMITIES	1 (0.1)
2.7.1.Vacuum therapy/ injuries in the leg / lower extremity amputation	1 (100)
3. OBSTACTLES RELATED TO THE RESOURCES	**12 (0.5)**
3.1.1.Absence of HOBE measurement device on the bed	10 (83.3)
3.1.2.Elevated nursing workload	2 (16.7)

HOBE: head-of-bed elevation

Factors related to SP compliance and HOBE

In the bivariate analysis of the factors related to SP compliance, as per observations, the only factor that showed a strong relationship was the ICU (Phi=0.304; p<0.001). Other variables showed moderate or little relationship, even if they were statistically significant. We did not identify nutrition, vasoactive drug requirements, obesity defined as Body Mass Index ≥30kg/m^2, hypotension (mean arterial pressure <65 mmHg) or high intra-abdominal pressure as significant determinants of SP compliance (Table 3-supplementary data).

As regards the factors related to HOBE, none showed a strong relationship. However, ICU (maximal mean difference 7.4º; p<0.001), high intracranial pressure with a monitoring catheter (mean difference 7.1º; p<0.001) were associated with higher HOBE degree and the vascular access used for continuous renal replacement (mean difference 7.0º; p<0.001) was associated to a lower HOBE degree. The vascular access for renal replacement associated with the lowest HOBE was the subclavian (n=47) [mean 20.3 (SD 5.1)º] followed by the femoral (n=605) [mean 27.0 (SD 6.0)º] and the jugular (n=203) [mean 27.4 (SD 6.6)º].

In the multivariate analysis the variables that remained significant evidencing an increased SP compliance were ICU, spontaneous ventilation mode, researcher staff nurse, intracranial pressure monitoring catheter, beds with HOBE device, medical, surgical or neurocritical diagnosis and higher patient age. Meanwhile the variables significantly associated with a decrease in SP compliance were lateral position, renal replacement therapy, nursing night shift, open abdomen, abdominal vacuum therapy and agitation (Table 4a). Similar results were observed in the multivariate analysis of the factors related to HOBE (Table 4b).

Table 4a. Multivariate logistic regression analysis of the factors related to the semi-recumbent position compliance.

	OR (CI95%)	P
ICU		**<0.001**
- ICU 1	1	
- ICU 2	7.32 (5.62-9.54)	**<0.001**
- ICU 3	1.54 (1.25-1.90)	**<0.001**
- ICU 4	1.98 (1.58-2.48)	**<0.001**
- ICU 5	2.15 (1.72-2.70)	**<0.001**
- ICU 6	0.98 (0.74-1.28)	0.856
Ventilation mode		**<0.001**
- Controlled	1	
- Spontaneous	1.21 (1.06-1.39)	**0.005**
- T-piece	2.52 (1.70-3.73)	**<0.001**
Nursing shift		**<0.001**
- Morning	1	
- Afternoon	0.88 (0.77-1.00)	0.055
- Night	0.61 (0.53-0.69)	**<0.001**
Nursing experience in critical care		**<0.001**
- < 1 year	1.23 (0.99-1.51)	0.053
- 1-5 years	1.17 (1.01-1.35)	**0.031**
- 6-10 years	1.41 (1.23-1.62)	**<0.001**
- > 10 years	1	
Level of sedation		**0.039**
- No sedation	1	
- Moderate sedation	0.83 (0.70-0.98)	**0.034**
- Deep sedation	1.04 (0.90-1.21)	0.543
Patient's age		**<0.001**
- ≤ 49 years	1	
- 50-59 years	1.19 (0.96-1.48)	0.107
- 60-69 years	0.95 (0.79-1.14)	0.600
- 70-79 years	1.01 (0.84-1.21)	0.923
- ≥ 80 years	1.48 (1.17-1.87)	**0.001**
APACHE II		

- <10 points	1	0.204
- 10-19 points	1.20 (0.96-1.51)	0.114
- 20-29 points	1.10 (0.86-1.39)	0.448
- > 30 points	1.27 (0.92-1.75)	0.146
Open abdomen	0.65 (0.50-0.85)	**0.002**
Abdominal vacuum therapy	0.59 (0.37-0.95)	**0.027**
Agitation	0.39 (0.28-0.54)	**<0.001**
Intracranial pressure catheter	3.03 (2.20-4.17)	**<0.001**
Medical diagnose	1.55 (1.30-1.84)	**<0.001**
Neurocritical diagnose	1.31 (1.04-1.64)	**0.019**
Surgical diagnose	1.26 (1.06-1.51)	**0.011**
Bed with HOBE measurement device	1.35 (1.11-1.63)	**0.002**
Investigator nurse	1.66 (1.46-1.88)	**<0.001**
Lateral position	0.79 (0.68-0.92)	**0.003**
Renal replacement therapy	0.56 (0.47-0.66)	**<0.001**

ICU: intensive care unit, HOBE: head-of-bed elevation, T-piece: spontaneous ventilation mode that is provided with a T-piece and it is used during weaning evaluation. APACHE II: severity score Acute Physiology And Chronic Health Evaluation II. Moderate sedation: The patient responds to verbal commands or is sleepy and awakes when hearing a voice. Deep sedation: The patient responds to sound or light but do not respond to any stimulus. OR>1 favors compliance, Characteristics of the model: X^2=1084.08; p<0.001; R^2 Nagelkerke=0.201; correctly prognosticated (positive: 70.8%; negative: 62.3%; global=66.9%); Constant of the model=-0.078,

Table 4b. Multivariate linear regression analysis of the factors related to the head-of-bed elevation

	Change in HOBE (º) (CI95%)	**P**
ICU		
- ICU 1	1	
- ICU 2	6.24 (5.59-6.90)	**<0.001**
- ICU 3	1.32 (0.74-1.89)	**<0.001**
- ICU 4	2.40 (1.77-3.02)	**<0.001**
- ICU 5	3.16 (2.57-3.75)	**<0.001**
- ICU 6	0.07 (-0.64-+0.77)	0.848
Bed with HOBE device	0.05 (-0.45-+0.56)	0.833
Nursing experience in critical care		
- < 1 year	0.48 (-0.08-+1.04)	0.093
- 1-5 years	0.40 (0.02-0.78)	**0.037**
- 6-10 years	1.20 (0.83-1.57)	**<0.001**
- >10 years	1	
Investigator nurse	1.26 (0.92-1.57)	**<0.001**
Ventilation mode		
- Controlled	1	
- Spontaneous	0.65 (0.27-1.02)	**0.001**
- T-piece	3.82 (2.89-4.75)	**<0.001**
Sat/FiO_2 (>300)	-0.39 (-0.71--0.074)	**0.016**
Sedation level		
- No sedation	1	
- Moderate sedation	-1.20 (-1.63--0.77)	**<0.001**
- Deep sedation	-0.57 (-0.97--0.17)	**0.005**
Agitation	-3.87 (-4.70--3.04)	**<0.001**
Intracranial pressure catheter	6.19 (5.35-7.03)	**<0.001**
Abdominal Vacuum therapy	-1.52 (-2.71--0.32)	**0.013**

Open abdomen	-1.34 (-2.10--0.58)	**0.001**
Renal replacement therapy	-2.15 (-2.61--1.70)	**<0.001**
Lateral position	-0.95 (-1.33--0.56)	**<0.001**
Obesity perceived by the nurse	0.30 (0.00-0.61)	**0.048**
Medical disease	0.98 (0.67-1.23)	**<0.001**
Patient >65 years old	-0.23 (-0.54-+0.08)	0.145

ICU: intensive care unit; HOBE: head-of-bed elevation; Sat/FiO_2: Oxygen Saturation / Fraction of inspired oxygen, T-piece: spontaneous ventilation mode that is provided with a T-piece and it is used during weaning evaluation. Moderate sedation: The patient responds to verbal commands or is sleepy and awakes when hearing a voice. Deep sedation: The patient responds to sound or light but do not respond to any stimulus. Characteristics of the model: R^2=0.216, F=78.283, p<0.001, Constant of the model=26.930,

Pressure ulcers and HOBE

Thirty-six patients developed PU (13.0%). However, the patients diagnosed with PU during the first day of admission were excluded due to the uncertainty of the relationship between HOBE and PU and as to whether the HOBE had been measured. Therefore only 25 (9.1%) patients with PU were included in the analysis. Their characteristics are shown in Table 5. These patients developed 34 PUs, 17 (68%) of them developing only one, 7 (28%) developing 2 and one (4%) developing 3. Twelve (35.3%) PUs were Stage I, 15 (44.1%) were Stage II and 7 (20.6%) Stage III. Most of them were diagnosed in the sacrum (52.9%), followed by the heel (41.2%) and the external malleolus (5.9%).

Table 5. Description of the patients' characteristics according to the presence of pressure ulcer.

	NO PU (n=240)	**PU (n=25)**	**P**
Age [median (P_{25}-P_{75})]	65.5 (55.0-75.0)	64.0 (48.0-76.0)	0.639
Gender (male) [n(%)]	166 (85.1)	20 (80.0)	0.260
APACHE II [median (P_{25}-P_{75})]	18.4 (14.0-24.0)	17.0 (12.0-20.0)	0.174
BMI (kg/m^2) [median (P_{25}-P_{75})]	27.7 (25.3-31.1)	28.4 (25.6-31.1)	0.609
Weight (kg) [median (P_{25}-P_{75})]	80.0 (70.0-90.0)	83.0 (70.0-95.0)	0.495
Diagnosis type [n(%)]			
- Medical	136 (56.7)	9 (36.0)	0.029
- Traumatic	14 (5.8)	2 (8.0)	0.653
- Neurocritical	34 (14.2)	1 (4.0)	0.218
- Surgical	89 (37.1)	15 (60.0)	**0.011**

Died [n(%)]	66 (27.5)	5 (20.0)	0.420
Pressure ulcer risk [n(%)]			
- Low risk	10 (4.2)	0 (0.0)	0.605
- Moderate risk	35 (14.6)	2 (8.0)	0.547
- High risk	195 (81.3)	23 (92.0)	0.271
Nutritional values [n(%)]			
- Albumin (g/dl)	2.32 (0.70)	1.78 (0.70)	**<0001**
- Pre albumin (g/dl)	14.1 (11.3-17.7)	11.0 (7.9-14.0)	**0.001**
- Proteins total (g/dl)	5.16 (0.86)	4.70 (0.87)	**0.011**
- Transferrin (mg/dl)	142.52 (39.87)	132.04 (33.70)	0.206
Mattress [n(%)]			
- Alternating pressures	213 (88.8)	22 (88.0)	1.000
- Viscoelastic	23 (9.6)	3 (12)	0.722
- Latex	4 (1.7)	0 (0.0)	1.000
Study days [median (P_{25}-P_{75})]	8.0 (4.0-13.5)	17.0 (9.0-27.0)	**<0.001**
MV days [median (P_{25}-P_{75})]	7.0 (3.0-12.0)	16.0 (9.0-26.0)	**<0.001**
ICU days [median (P_{25}-P_{75})]	12.0 (6.0-19.5)	22.0 (11.0-35.0)	**0.001**
SP compliance (%) [mean (SD)]	53.87 (26.60)	51.22 (31.38)	0.642
Head-of-bed elevation (º) [mean (SD)]	30.05 (4.07)	29.57 (4.07)	0.576
Obs MAP <70 (%) [median (P_{25}-P_{75})]*	6.3 (0.0-20.0)	20.0 (0.0-33.3)	**0.051**
Obs vasoactive drugs (%) [median (P_{25}-P_{75})]*	46.4 (6.0-87.1)	90.0 (26.9-100.0)	0.070
Obs sedation (%) [median (P_{25}-P_{75})]*	72.8 (40.6-95.4)	100.0 (86.7-100.0)	**<0.001**

BMI: body mass index; MV: mechanical ventilation; ICU: intensive care unit; SP: semi-recumbent position; Obs: Observation; MAP: mean arterial pressure. APACHE II: severity score Acute Physiology And Chronic Health Evaluation II. The values from the group with pressure ulcers correspond to the previous from the diagnosis *The variables related to the observations (measurements of the HOBE) correspond to the percentage of observations in which the patient had a MAP <70, vasoactive drugs or with sedation (regardless of the degree).

Table 5 shows a comparison of patient characteristics with and without PU. The diagnosis of PU did not affect HOBE as it remained similar to how it was previously (before diagnosis mean 29.6 (SD 4.6)º vs after diagnosis mean 29.9 (SD 4.0)º; p=0.677). In the multivariate analysis, HOBE was not related to the risk of PU. However, MV days, ICU days, length of sedation, vasoactive drugs and hypotension were evidenced as risk factors for PU development. Meanwhile an increased

APACHE II score and higher concentrations of albumin and pre-albumin showed up as preventive factors (Table 6).

Table 6. Multivariate logistic regression analysis for the factors related to the incidence of pressure ulcers.

	OR (CI 95%)	P
APACHE II score*	0.87 (0.83-0.92)	**<0.001**
Medical diagnosis	0.51 (0.23-1.09)	0.506
Surgical diagnosis	1.52 (0.69-3.33)	0.292
Albumin*	0.62 (0.39-0.98)	**0.041**
Pre albumin*	0.87 (0.82-0.93)	**<0.001**
Proteins*	0.93 (0.65-1.34)	0.695
MV days*	1.03 (1.00-1.06)	**0.029**
ICU days*	1.02 (1.01-1.04)	**0.014**
Obs sedation (%)$*	1.02 (1.01-1.03)	**<0.001**
Obs vasoactive drugs (%)$*	1.02 (1.02-1.03)	**<0.001**
Obs MAP < 70 (%)$*	1.02 (1.01-1.03)	**0.004**
Head-of-bed elevation (º)*	0.96 (0.90-1.02)	0.164

MV: mechanical ventilation; ICU: intensive care unit; MAP: mean arterial pressure. APACHE II: severity score Acute Physiology And Chronic Health Evaluation II. $The variables related to the observations (measurements of the HOBE) correspond to the percentage of observations in which the patient had a MAP <70, vasoactive drugs or with sedation (regardless of the degree). OR>1 pressure ulcer risk factor. Weighted analysis (Weight rule=9,6). Model characteristics: X^2: 238.459 p<0.001. R^2 Negelkerke=0.522. Correctly prognosticated (positive= 84.0%, negative= 79.6%; global= 81.8%).

DISCUSSION

This study is the first to evaluate the factors relating to SP compliance in such a broad scope and with a 28-day follow-up. Other studies with similar objectives have had a shorter follow-up of seven days [13,34]. The main findings of this investigation are, firstly, the heterogeneity of SP compliance according to the ICU, secondly, the gap that exists between guidelines, upcoming evidence with regard

to possible contraindications for SP and clinical practice, and thirdly, the absence of any association between HOBE and PU development.

The mean HOBE is below optimal despite being very close to the lower limit of 30º, which is consistent with the previous literature [13,16]. Better results were observed in smaller ICUs (ICU 2 and ICU 5), which have only 8 beds. Although not described previously, this result could be explained by the results from Labeau *et al.*, who evidenced better scores in a knowledge test of ventilator-associated pneumonia prevention guidelines in small ICUs like those cited [35,36]. The difference observed between different ICUs has been reported by other multicenter studies with similar objectives [13,15,34]. None of the studies gave clear causes due to the involvement of several levels of care beyond the scope of the research, such as organizational, structural and staff-related factors*.,* In a questionnaire to investigate the reasons for non-compliance, Kiyoshi *et al.* showed that professional attitudes with regard to the recommendation were associated with increased compliance [37]. Therefore participating in guideline development and understanding the rationale behind the measure to be implemented could be instruments to help increase adherence.

When staff nurses were asked, the most important causes of non-compliance were the visual perception of the staff nurse and the fact that the bed device for HOBE measurement indicated 30º. The evidence regarding visual perception is controversial as the literature differs [16,19,38,39], so only the result obtained from the BOSCH GLM80® was considered regardless of the bed device. This could have introduced a bias, as the nurses relied on the bed device. However, in order to maintain an accurate methodology, only the BOSCH device could be considered.

Indeed, when analyzing the measurements where this difference was observed, the HOBE ranged from 18.8º to 29.9º, indicating that the bed device is probably not reliable and should be considered with caution when it comes to monitoring SP compliance. Therefore when using these devices, clinicians should be careful to override the 30º mark. All beds had similar devices to the one shown in Figure 1.

With regard to the factors associated with SP compliance and HOBE, we found similar results to those in other studies [13,16,40,41].

It has been observed that beds with a HOBE measuring device increase SP compliance, and this coincides with the previous literature [40,42]. However, this result was not evidenced in all the participating ICUs. In UCI 1 there was higher SP compliance in patients looked after on beds without this device, in line with previous results [25]. When the staff nurses were asked about this result, they explained that visual perception was different depending on bed type, which supports the importance of visual perception with regard to the patient's comfort in SP compliance.

Nutrition, vasoactive drugs, obesity and abdominal hypertension have not been associated with SP compliance or HOBE elevation. Some studies have described different findings that show decreased compliance when the patient was overweight [19] and on vasoactive drugs [12,40,43], and increased compliance when the patient was receiving nutrition [13,19]. The relationship between intra-abdominal pressure and SP compliance had not previously been evaluated. Yi *et al.* showed that higher intra-abdominal pressure increases patient mortality and morbidity and described a significant positive correlation between intra-abdominal pressure and HOBE, concluding that the patient's position should be

considered in cases of high intra-abdominal pressure [44]. However, so far this recommendation seems not to have made the transition into clinical practice despite the fact that lower HOBE and SP compliance has been described in patients undergoing abdominal vacuum therapy or with an open abdomen, and most studies evaluating SP considered it an exclusion criterion [7,10,34,45].

In clinical practice, renal replacement therapy with a femoral catheter appears to be a challenging condition in which to achieve SP compliance. In two studies this was defined as a contraindication for SP, even though it is not present in the guidelines [13,45]. We therefore expected to evaluate clinical practice in relation to this issue. However, use of a vascular catheter for renal replacement could not be included in the multivariate analysis due to the low number of observations (n=855) compared to the general sample (n=6894). In addition, the results obtained were unexpected. The hypothesis was that the vascular access with the lowest HOBE would be the femoral, but instead it was the subclavian. Nonetheless, this result should be considered with caution due to sample heterogeneity.

Because there are multiple factors that influence SP compliance and could have a potential negative effect on patients' outcomes, clinical guidelines should take these disagreements into account and formulate clear contraindications for SP rather than issue a general recommendation.

The risk of pressure ulcers appears to be the other big obstacle to SP compliance for nurses, according to the literature [21] and clinical practice. 9.1% of patients developed PUs in this study (n=25) and this is the highest proportion of reported in studies assessing the association between HOBE and PU risk. Even so, we could find no relationship between HOBE and the risk of PU, although it would seem

logical to find a positive correlation between interphase pressure at the sacrum and HOBE [46], which is the main element for developing a PU [22]. We believe that ICU might play an important role that could not be evaluated due to the small sample size. A study with a bigger sample size and preferably less variability between centers could throw some light on this question. We did, however, successfully find PU risk factors as being low nutritional values, days of ICU admission, MV days, length of sedation, vasoactive drugs and hypotension, which is consistent with the previous literature [22,47,48].

We acknowledge that our study has a number of limitations. First, we recognize that in order to investigate the reasons for non-compliance according to nurses, a qualitative design could have given a deeper perspective. However, due to the multicenter design and the number of observations, we considered that it was more important to get the information from all possible observations directly when non-compliance was observed, rather than conducting focus groups, for example. Nonetheless, the researchers did create a questionnaire that was distributed to healthcare professionals to find out about their perceptions [49]. Second, 36.7% of the measurements obtained in the study were from patients cared for by researcher nurses. We are aware that this could introduce a strong bias into the study results. However, the nature of the study made it very difficult to overcome this limitation as researchers had to be available 3 times a day and 7 days a week for 9 months, with no external researchers available. Third, for PU analysis, almost a third of the sample was excluded because the diagnosis of PU was made during the first day of the study. And finally, approximately 70 researchers were needed in order for the study to be carried out correctly, and this could introduce a bias. However, the principal investigator trained all the research

team and provided the necessary guidelines to minimize bias, and each center had its own referral researcher. Third, the sample size calculation was performed for the main objective of the study and there was no sample calculation for the analysis of PU due to the unknown prevalence in the participating centers. Therefore, the multivariate analysis performed with regards to the relationship between HOBE and PU might be underpowered according to Mallet S, et al. [50]. Thus, a bigger sample should be recruited to confirm or refuse the results obtained in our analysis.

CONCLUSIONS

Semi-recumbent positioning compliance is below optimal despite the fact that it seems achievable most of the time in ICUs. Factors that affect SP compliance include the ICU, abdominal conditions, renal replacement therapy, agitation and bed type. The present study suggests that HOBE does not increase the risk of PU. Efforts should be made to clarify SP contraindications, and further analysis of its safety profile is needed.

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***Response to Reviewers**

First of all, we would like to thank all the comments provided to improve the manuscript. All modifications made in the manuscript are highlighted in yellow.

We will response point by point to all questions asked:

Initial comments:

*** All full papers must have an abstract. For research and review papers this must be structured**

The manuscript already has an structured abstract (background, objectives, methods, results and conclusions)

*** For research and review papers, the title should be in the format 'Topic / question: design/type of paper'**

The title of the manuscript already follows the recommendation as can be seen: “Related factors to semi-recumbent position compliance and pressure ulcers in patients with invasive mechanical ventilation: an observational study. (CAPCRI study)”

*** Research and review must include short bullet points for 'what is already known and 'what this paper adds' (up to 3 bullets for each)**

The sections of “what is already known and what this paper adds” has been structured in bullet points.

*** All full papers must be accompanied by a completed author checklist, available to download in the Guide for Authors (http://cdn.elsevier.com/promis_misc/IJNSchecklist2.doc) - please upload the word document as a separate file**

The checklist has been updated and uploaded.

*** All research and review papers must be checked against the relevant reporting guidelines**

The checklist has been updated and uploaded.

*** The journal strongly discourages the use of abbreviations (including acronyms and initials). Use only abbreviations that are universally used and only when absolutely necessary.**

The abbreviations have been reviewed and reduced.

Finally we ask that you closely proof read and check the use of English in the manuscript. This makes it far easier for reviewers to make clear recommendations based upon the scientific merit of your paper and avoids requests for further revision if the science is acceptable.
The manuscript has been proof read and checked the English.

Reviewer comments:

COMMENT FROM ASSOCIATE EDITOR: Thank you very much for submitting your work to the IJNS. In addition to the reviewer comments please pay careful attention to the author instructions.

- Please use abbreviations sparingly and avoid acronyms as much as possible (e.g. MAP, IAP etc). Please also check the tables (e.g. what is a T-piece, sat/FiO2 etc.). While many readers will know these abbreviations, many will not.

The number of abbreviations has been reduced. The following abbreviations have been deleted: VAP, BMI, MAP, IAP. In the new version, only the most frequent abbreviations appear on the text: ICU, SP, HOBE, MV.

However, in tables, the abbreviations are still present due to the available space but on the legend are defined all the abbreviations used. Acronyms like Sat/FiO2 and APACHE II have been defined in table legends as well as T-piece has been explained.

- You structured your manuscript according STROBE. Please indicate the page numbers where you addressed the items instead of using crosses. Please expand the item #8. Please clearly describe ALL instruments used, e.g. APACHE later appearing in the table. Please also address items #9 and #15.

The item 8 has been described deeply in methods section and accompanied by more information in supplementary data because we thought it would be easier for the reader.

The item 9 has been included in the methods section.

We believe that the item 15 is already included in all the results section. More importantly, in pages 9-10 for semirecumbent position outcomes and 15 for pressure ulcers outcomes.

Reviewer #1:

The authors performed a prospective multicentre cohort study to assess adherence with the semi-recumbent positioning recommendation and the relationship with pressure ulcers. I have the following comments...
1) Abstract: the abstract states... "The diagnosis of PUs did not affect the head-of-bed elevation." But according to the objectives of the study it is the other way around: "Head-of-bed elevation was not associated with risk of PU development" (unless the investigators want to report whether nurses considered the existence of PUs in their decision to perform HoB elevation).

The analysis of the relationship between pressure ulcers and head-of-bed-elevation intended to find out if the head-of-bed elevation had any impact on the risk of PU. However, on the other hand, we analysed the impact of the diagnosis of a PU to the head-of-bed elevation to know if the attitude from nurses changed. We acknowledge that this could be confusing when analyzing the conclusions from the abstract and objectives. We added this objective in the abstract and in the manuscript.

2) Background - 1st paragraph: From what the authors write it is clear that exists at least some controversy about the issue of semirecumbent positioning (for whaztever reson, either effectiveness to reduce VAP risk or in terms of feasibility); for that reason a reference focused on the controversial aspects of VAP prevention would be better placed here (e.g. Lorente L, et al. Am J Respir Crit Care Med 2010).

The reference has been added.

3) Please clarify: the inclusion criterion "requiring >48 hrs of MV"... was this an anticipated estimate that the patient probably needed >2 days of MV or were patients only included when they were already for 2 days on the ventilator?

A clarification has been included in the Methods section regarding this point:

To ensure the collection of the HOBE from the first 24h of MV, patients were included as soon as possible and if they were under MV less than 48 hours were excluded.

4) What is meant by "the complexity of the centers"?

This sentence has been changed to avoid confusion. The new version is:

The level of care of the centers were 2a and 2b corresponding to high or moderate complexity of care.

The assignation of the centers is made by the Catalan Government and it is referenced in the text. The document is made for the assistance of politraumatic patients but is applicable to all patients because they describe the requirements of the centers to belong to the different levels of care.

5) What is meant by "collection rate, 86,3%"? Does this mean that 13,7% of presumed HoBe evaluations were not performed? If so, is this corrected for the fact that when patients are extubated after 1 measurement it is normal that the two other (for that day) are not needed.

The collection rate means the measurements obtained from all possible measurements (considering all measurements where the patient was with MV and was in the ICU on the bed). If the patient was extubated, the following measurements were not performed per protocol.

This has been clarified on the Methods section of the manuscript: *HOBE was determined 3 times per day (one time per nursing shift) while the patient was under MV or T-piece for weaning evaluation and present in the ICU lying on the bed.*

6)Table 1 : the ** part of the table: do the n (%) represent the number and % of the HOBE measurements?

Yes, the measurements with those nurses characteristics.

7) IMPORTANT: the authors reported failure to adhere with the HOBE recommendation when this was <30°. However, the trial by Van Niewenhove et al. demonstrated that there was no difference in VAP when a group with about 11° (assumed to be 30°) was compared with 28° (assumed to be 45°). Therefore I would like to know the % of patients/measurements in which the HOBE was <10° because this is probably the critical threshold.

There were only 10 (0.14%) measurements ≤10º from all 6894 observations. The minimum HOBE was 4.0º and the maximum of this group was 10.0º. The mean elevation within this group was 8.7º (SD 1.97º).

8) Table 3: do I miss the only strong factor related with SP compliance (ICU)?

Thanks for this really important comment. This was missing and it has been included. Thank a lot for discovering this relevant mistake.

9) Vascular access and PS compliance: there is no meaningful rational between subclavian/jugular access and lower HOBE; the only factor that might have been related is femoral access as it might have lead to occlusion.

We acknowledge that this is a limitation of the study as it is discussed in page 20 of the manuscript. We could not conclude anything else due to the small sample of femoral access. On the other hand, other factors might play a role because many times in clinical practice jugular access has complications with renal replacement therapy due to anatomical issues. However, all the potential factors influencing this relationship are out of our control.

10) In reporting on multivariate analysis in the text do mention as well in which direction the variable is associated with increasing SP (e.g. ventilation mode: the higher the patients' independcy the higher the SP compliance). This will make the paper more easily to read/understand.

The text has been clarified in different parts of the results sections. Changes are highlighted in yellow.

11) Table 4a: which ICU did you take as reference category? The one with the largest sample?

The ICU taken as reference is ICU 1. This was chosen because it was the one with the lowest HOBE and SP compliance and it was easier to show the results.

12) Table 5: I assume that "No UPP" means "No pressure ulcer"...?

Yes. Thanks for the appreciation, this was a translation oversight.

13) Table 6 and related text in the Results: please confirm it are HIGH concentrations of albumin and pre albumine that are related with the incidence of PUs (and not vice versa). Also when were (pre) albumine levels recorded? On admission only, for example...?

In the related text it is stated that albumin and pre-albumin are shown to be preventive factors for PU. And in table 6, in the legend it states OR >1 is a risk factor for PU. And Albumin and Pre-albumin have OR <1. Therefore, having higher values of albumin and pre-albumin are preventive factors for PU development. On the other hand, the values recorded are the ones prior to PU diagnosis. We recorded weekly values and the values included in the model are the last available before the diagnosis.

14) Discussion: page 18, line 11: omit the word "massive"

Word deleted.

15) Discussion: page 19, line 18-20: Rephrase: "...% of patients developed PUs in this study (n=25) and this is the highest proportion of reported in studies assessing the association between HOBE and PU risk."

This sentence has been rephrased according to your recommendation.

Reviewer #2: Many thanks for this well written article, it is clearly presented and easy to read and understand. The one comment I have relates to the sample size calculation, this has been undertaken with regard to SP, not with regard to the development of pressure ulcers. Thus,the regression may be under-powered for inference pertaining to pressure ulcers, given the requirement for 10 incidences of pressure ulcer per variable. The regression includes 12 variables, thus 120 pressure ulcer incidences would be needed, using the rule of ten (Mallett S, Royston P, Dutton S, Waters R, Altman DG. Reporting methods in studies developing prognostic models in cancer: a review. BMC Med 2010;8:20). This point needs to be addressed within the paper.

Thanks for this relevant consideration. This aspect has been addressed in the limitations sections:

Third, the sample size calculation was performed for the main objective of the study and there was no sample calculation for the analysis of PU due to the unknown prevalence in the participating centers. Therefore, the multivariate analysis performed with regards to the relationship between HOBE and PU might be underpowered according to Mallet S, et al. [45]. Thus, a bigger sample should be recruited to confirm or refuse the results obtained in our analysis.

AUTHOR COMMENTS:

- We included in table 4b the information from the Bed with HOBE device which was missing by mistake.

Supplementary Material

Click here to download Supplementary Material: SUPPLEMENTARY DATAv2.docx