CHEST

Original Research

PULMONARY VASCULAR DISEASE

Use of Intermittent Pneumatic Compression and Not Graduated Compression Stockings Is Associated With Lower Incident VTE in Critically Ill Patients

A Multiple Propensity Scores Adjusted Analysis

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Background: **A limited amount of data exist regarding the effect of intermittent pneumatic compression (IPC) and graduated compression stockings (GCS) on the incidence of VTE in the ICU setting. The objective of this study was to examine the association of mechanical thromboprophylaxis with IPC or GCS with the risk of VTE and hospital mortality among critically ill medical-surgical patients.**

Methods: **In this prospective cohort study of patients admitted to the ICU of a tertiary-care medical center between July 2006 and January 2008, we used multiple propensity scores adjustment to examine the association of IPC and GCS with VTE. The primary outcome was incident VTE, including DVT and pulmonary embolism. The following data were collected: patient demographics, admission physiologic data, VTE risk factors, pharmacologic thromboprophylaxis, and mechanical thromboprophylaxis.**

Results: **Among 798 patients enrolled in the study, incident VTE occurred in 57 (7.1%). The use of IPC was associated with a significantly lower VTE incidence compared with no mechanical thromboprophylaxis (propensity scores adjusted hazard ratio, 0.45; 95% CI, 0.22-0.95; *P* = .04). GCS were not associated with decreased VTE incidence. No significant interaction was found between the mechanical thromboprophylaxis group and the type of prophylactic heparin used (*P* = .99), recent trauma (*P* = .66), or recent surgery (*P* = .07) on VTE risk.**

Conclusions: **The use of IPC, but not GCS, was associated with a significantly lower VTE risk. This association was consistent regardless of the type of prophylactic heparin used and was not modified by trauma or surgical admission.**

CHEST 2013; 144(1):152–159

Abbreviations: ACCP = American College of Chest Physicians; ACP = American College of Physicians; aHR = adjusted hazard ratio; CLOTS = Clots in Legs or Stockings after Stroke; GCS = graduated compression stockings; HR = hazard ratio; IPC = intermittent pneumatic compression; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; RCT = randomized controlled trial; UFH = unfractionated heparin

VTE, including DVT and pulmonary embolism (PE), is a common complication of critical illness[1] and is associated with significant morbidity and mortality.[1,2] Thromboprophylaxis given to all critically ill patients has become the standard of care and is supported by clinical practice guidelines.[3] It also has been incorporated into public reporting, regulatory agency priorities, and national quality initiative priorities. According to the "National Voluntary Consensus Standards for Prevention and Care of Venous Thromboembolism," VTE is considered the most common preventable cause of hospital deaths in the United States.[4] The Agency for Healthcare Research and Quality has prioritized thromboprophylaxis as the number one patient safety practice among nearly 70 practices.[5] The Centers for Medicare & Medicaid Services has designated VTE that is not present on admission but subsequently occurs during the hospital stay as a hospital-acquired condition and will not pay for the expenses associated with it.[6]

Pharmacologic prophylaxis has been recommended as the thromboprophylaxis of choice in critically ill patients[7]; however, VTE continues to occur. For example, in one study, VTE occurred in 5.1% and 5.8% of patients with critical illness not related to trauma receiving dalteparin or unfractionated heparin (UFH), respectively.[7]

Unlike for pharmacologic thromboprophylaxis, limited data exist on the efficacy of mechanical thromboprophylaxis, including intermittent pneumatic compression (IPC) and graduated compression stockings (GCS).[8,9] These observational studies were limited by small sample sizes, heterogeneous patient populations, and variation in end points. Existing randomized controlled trials (RCTs) and a subsequent meta-analysis compared mechanical devices to pharmacologic thromboprophylaxis[10,11] as the primary prophylactic regimen, a question of little clinical relevance at present. To our knowledge no study has reported the effect of IPC and GCS on incident VTE in a mixed medical-surgical ICU setting in which pharmacologic thromboprophylaxis is used. The lack of clear evidence is reflected by the wide variability in the use of these devices in surveys from Canada, France, Australia, and Germany[10,12-15] and, more importantly, in the current practice guidelines. The American College of Physicians (ACP) guidelines for nonsurgical patients recommend against the use of GCS and suggest that IPC be used as an alternative to pharmacologic thromboprophylaxis but made no recommendation about its adjunct use with pharmacologic thromboprophylaxis.[8] The eighth edition of the American College of Chest Physicians (ACCP) guidelines recommended that GCS or IPC be used as an alternative or adjunct to pharmacologic thromboprophylaxis.[16] The recent, ninth edition of the ACCP guidelines recommend the use of GCS or IPC (although preference is given to IPC) as an alternative, but not as an adjunct, to pharmacologic thromboprophylaxis in nonsurgical critically ill patients.[3] In surgical, nonorthopedic patients (presumably critically ill included), the ACCP guidelines recommend that mechanical thromboprophylaxis (preferably with IPC) be used as an alternative or adjunct to pharmacologic thromboprophylaxis.[17] However, in general orthopedic patients (presumably critically ill patients included), the ACCP recommends IPC as an alternative or adjunct, but no recommendation is made regarding GCS.[18] With consideration of the limited data and the differences in clinical practice guidelines, we studied the association between the use of mechanical thromboprophylaxis with IPC or GCS and the risk of VTE and hospital mortality among critically ill medical-surgical patients.

Materials and Methods

Subjects and Setting

This prospective, observational, cohort study was conducted in the adult medical-surgical ICU at King Abdulaziz Medical City, a tertiary-care academic medical center in Riyadh, Saudi Arabia. Consecutive patients admitted to the ICU from July 2006 to January 2008 were enrolled in the study if they were aged ≥ 18 years with an expected ICU length of stay of > 48 h. The following patients were excluded: those with a do not resuscitate order or brain death, those receiving long-term therapeutic anticoagulation with warfarin or heparin, and those admitted to the ICU with acute PE or DVT diagnosed on or within the first 24 h of ICU admission. The study was approved by the institutional review board of the hospital (IRBC/016/2006), and informed consent was not required.

The ICU is run as a closed unit by on-site, critical care, board-certified intensivists.[19] In 2004, the hospital created a multidisciplinary task force chaired by the primary author (Y. M. A.) to develop hospital-wide guidelines for thromboprophylaxis. The guidelines were based on the seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy.[20] Implementation of the guidelines included several educational awareness days directed to all physicians and nurses in the hospital along with the distribution of posters and pocket-sized summaries of the guidelines. In the ICU, a checklist for thromboprophylaxis was incorporated in the admission order set and in the template of the daily progress notes.

Interventions

The IPC devices used during the study period were sequential and multichamber (Kendall SCD Response and SCD Express Compression System Controllers; Covidien). The consumption records indicated that the sleeves used were below knee in 94% of the patients, with the rest being thigh length. The GCS used were primarily below knee (85.4%). The length of IPC sleeves and GCS was determined by the bedside nurse. Fitting instructions from the manufacturers were used to select and apply GCS. GCS were discontinued during ICU stay only if the patient declined to wear them or there was concern about skin integrity.

Measurements

The following data were collected: patient demographics, including age and sex; admission physiologic data; VTE risk factors; pharmacologic thromboprophylaxis; and mechanical thromboprophylaxis (IPC and GCS) (Table 1). Of the 798 enrolled patients, 389 did not receive mechanical thromboprophylaxis, 211 received IPC, 153 received GCS, and 45 received both modalities. Of the patients receiving both modalities, 18 were assigned to the IPC group and 27 to the GCS group on the basis of which device was

Manuscript received August 15, 2012; revision accepted December 21, 2012.
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Funding/Support: The study was sponsored in part by an unrestricted grant from sanofi-aventis, Saudi Arabia.
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DOI: 10.1378/chest.12-2028

Table 1—*Characteristics of the Patient Cohort and the Study Groups*

Variable	All Patients (N = 798)	IPC (n = 229)	GCS (n = 180)	No Mechanical Thromboprophylaxis (n = 389)	Crude *P* Value	Propensity Score Adjusted *P* Value
Age, y	50.2 ± 21.2	47.4 ± 21.6	49.0 ± 21.5	52.3 ± 20.7	.15	1.00
Female sex	263 (33.0)	71 (31.0)	50 (27.8)	142 (36.5)	.09	.67
Time in hospital prior to enrollment, d	10.6 ± 29.6	9.3 ± 24.7	7.6 ± 25	12.8 ± 33.7	.0001	.20
Admission physiologic data						
APACHE II score	24.0 ± 9.0	24.2 ± 9.3	23.3 ± 8.5	24.2 ± 9.1	.53	.99
Glasgow coma score	8.6 ± 4.1	7.4 ± 3.8	8.4 ± 3.9	9.4 ± 4.2	< .001	1.00
Creatinine, μmol/L[a]	158.9 ± 144.7	142.5 ± 119.3	151.9 ± 153.1	171.9 ± 153.1	.04	1.00
Platelets, × 10^9/L	244.4 ± 155.6	225.0 ± 131.3	277.3 ± 127.7	253.0 ± 162.3	.18	.98
INR	1.4 ± 0.7	1.4 ± 0.8	1.4 ± 0.7	1.4 ± 0.7	.65	1.00
PTT, s	42.4 ± 60.2	43.3 ± 51.9	43.3 ± 54.8	41.4 ± 66.8	.90	1.00
Specific risk factors for VTE						
Trauma	226 (28.3)	85 (37.1)	61 (33.9)	80 (20.6)	< .001	.98
Femur or pelvic fracture or hip or knee replacement	52 (6.5)	11 (4.8)	11 (6.1)	30 (7.7)	.36	1.00
Bedridden status > 3 d	394 (49.4)	104 (45.4)	75 (41.7)	215 (55.3)	.004	1.00
Malignancy	94 (11.8)	32 (14.0)	24 (13.3)	38 (9.8)	.22	1.00
Recent surgery	243 (30.5)	91 (39.7)	49 (27.2)	103 (26.5)	.001	.92
Previous VTE	12 (1.5)	3 (1.3)	2 (1.1)	7 (1.8)	.79	.93
Sepsis	168 (21.1)	48 (21.0)	34 (18.9)	86 (22.1)	.68	.88
Use of vasopressors	408 (51.1)	127 (55.5)	96 (53.3)	185 (47.6)	.13	.87
PRBC transfusion	390 (48.9)	132 (57.6)	74 (41.1)	184 (47.3)	.003	.94
Central venous catheter	595 (74.6)	178 (77.7)	147 (81.7)	270 (69.4)	.003	1.00
Hemodialysis catheter	158 (19.8)	45 (19.7)	32 (17.8)	81 (20.8)	.70	1.00
Prophylactic UFH	411 (51.5)	97 (42.4)	80 (44.4)	234 (60.2)		
Prophylactic enoxaparin	137 (17.2)	45 (19.7)	38 (21.1)	54 (13.9)		
Both[b]	91 (11.4)	35 (15.3)	27 (15.0)	29 (7.5)	.000	.87
No pharmacologic thromboprophylaxis	159 (19.9)	52 (22.7)	35 (19.4)	72 (18.5)		
Therapeutic anticoagulation after enrollment	67 (8.4)	19 (8.3)	7 (3.9)	41 (10.5)	.03	.03

Data are presented as mean ± SD or No. (%). Concomitant use of prophylactic UFH and enoxaparin is shown among the three groups of mechanical thromboprophylaxis used. APACHE = Acute Physiology and Chronic Health Evaluation; GCS = graduated compression stockings; INR = international normalized ratio; IPC = intermittent pneumatic compression; PRBC = packed RBC; PTT = partial thromboplastin time; UFH = unfractionated heparin.

[a]To convert conventional units to mg/dL, divide by 88.4.

[b]Both refers to the administration of UFH and enoxaparin at different periods of the ICU stay.

used ≥ 50% of the time in the ICU. Follow-up sensitivity analysis allocating patients who received both modalities alternatively to the IPC on GCS groups did not show any significant difference in the results. Two patients had equal participation and were randomly assigned to either the IPC or the GCS group.

Study End Points

The primary end point was incident VTE (lower extremities DVT, PE, or both) during the ICU stay and up to 5 days after ICU discharge. Diagnostic tests were performed at the discretion of the treating team and included Doppler ultrasonography for the diagnosis of DVT and spiral CT scan of the chest and ventilation-perfusion scanning of the lungs for PE. Hospital mortality was the secondary end point.

Statistical Analysis

Continuous variables are reported as mean ± SD and categorical variables as counts and proportions. Comparison among groups (IPC, GCS, and no mechanical thromboprophylaxis) was done with analysis of variance, Kruskal-Wallis test, multinomial logistic regression, or χ^2 test, as appropriate. Because of the observed imbalances in baseline characteristics, the multiple propensity scores adjustment approach[21] was used as detailed elsewhere.[22] Three investigators (Y. M. A., M. K., S. I. D.) selected variables for the final model to drive propensity scores, which was done according to the findings of Brookhart et al.[23] These variables were age, sex, time spent in the hospital prior to enrollment, APACHE (Acute Physiology and Chronic Health Evaluation) II score, Glasgow coma score, creatinine level, international normalized ratio, partial thromboplastin time level, recent trauma, recent femur or pelvic fractures or knee or hip replacement, bedridden status, presence of malignancy, recent surgery, packed RBC transfusion, presence of central venous or hemodialysis catheter, presence of sepsis, use of vasopressors, use of prophylactic UFH or enoxaparin, and use of therapeutic anticoagulation after enrollment. Because mechanical device categories (IPC, GCS, and no mechanical thromboprophylaxis) numbered more than two (the dependent variable), multinomial logistic regression analysis was carried out with the aforementioned selected variables as independent variables. The likelihood ratio test for the model, compared with the empty model, was assessed.

Independence of irrelevant alternatives assumption and goodness of fit were checked with the Hausman and McFadden[24] and Hosmer-Lemeshow[25] generalized goodness-of-fit tests, respectively. Three separate propensity scores were then derived from the model. Overlap of different propensity scores was checked visually with the box plot method.[22] To check the balancing effect of propensity scores, two of three multiple propensity scores and their mutual interactions were used as covariates in an analysis of covariance for continuous variables and in multinomial logistic regression for categorical variables.

Finally, Cox regression analysis was done to estimate the crude and adjusted associations of IPC and GCS (compared with no mechanical thromboprophylaxis) on the occurrence of VTE. Three different adjusted models were performed including the two propensity scores, the selected variables mentioned earlier, or both. Results are reported as hazard ratios (HRs) with corresponding 95% CIs and associated *P* values. Wald test was used to investigate the presence of a significant interaction between the use of a mechanical device (IPC, GCS, or no mechanical thromboprophylaxis) and the type of prophylactic heparin used (UFH, enoxaparin, or none), recent trauma, and admission as a surgical patient. All tests were considered significant at the $< .05$ α level. Stata version 11 SE for Windows (StatCorp LP) was used in all analyses.

Results

General

The baseline characteristics and main VTE risk factors are shown in Table 1. The mean age was 50.2 ± 21.2 years. The first day mean APACHE II score was 24.0 ± 9.0. Of note, 28% of patients were admitted because of trauma, 31% had recent surgery, and 51% were receiving a vasopressor. Central venous catheterization was common either for IV access (75%) or hemodialysis (20%).

Exposures

The IPC group comprised 229 patients (28.7%), the GCS group comprised 180 patients (22.6%), and the no mechanical thromboprophylaxis group comprised 389 patients (48.7%). Concomitant pharmacologic thromboprophylaxis with UFH or enoxaparin is shown in Table 1.

Propensity Scores

The balancing effect of the generated propensity scores is shown in Table 1. When adjusted to propensity scores, all baseline characteristics were balanced. The only exception was the use of therapeutic anticoagulation after enrollment. This variable was also included from the multivariate model and showed no impact on effect estimates of the association of IPC or GCS with VTE. Box plots for the overlap of the three propensity scores among the three study groups are shown in Figure 1.

Outcomes

Incident VTE occurred in 57 patients (7.1%), with 11 in the IPC group (4.8%), 18 in the GCS group

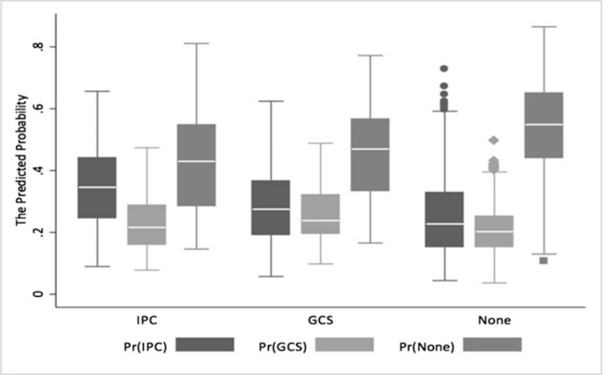

Figure 1. Box plots for overlap of the multiple propensity scores among the three groups of devices used. GCS = graduated compression stockings; IPC = intermittent pneumatic compression; None = no mechanical thromboprophylaxis; Pr = propensity score.

(10.0%), and 28 in the no mechanical thromboprophylaxis group (7.2%) (Table 2). A crude analysis showed that IPC use was associated with a significantly lower VTE risk (HR, 0.48; 95% CI, 0.24-0.97; *P* = .04). No significant change in this estimate was observed with propensity score adjustment (adjusted hazard ratio [aHR], 0.45; 95% CI, 0.22-0.95; *P* = .03), multivariate adjustment (aHR, 0.45; 95% CI, 0.21-0.94; *P* = .04), or both combined (aHR, 0.45; 95% CI, 0.22-0.95; *P* = .04). No significant association between the use of GCS and VTE was noticed in either crude (HR, 1.15; 95% CI, 0.64-2.08; *P* = .64), propensity score adjustment (aHR, 1.09; 95% CI, 0.59-2.04; *P* = .76), multivariate adjustment (aHR, 1.13; 95% CI, 0.60-2.12; *P* = .7), or both propensity score and multivariate adjustment combined (aHR, 1.24; 95% CI, 0.66-2.34; *P* = .5) (Fig 2, Table 3). No significant interaction was found between the mechanical thromboprophylaxis groups and the type of prophylactic heparin used (*P* = .99), recent trauma (*P* = .66), or recent surgery (*P* = .07)

The association of mechanical thromboprophylaxis with hospital mortality was not significant on crude or adjusted analyses for either IPC (propensity score aHR, 0.92; 95% CI, 0.68-1.24; *P* = .59) or GCS (propensity score aHR, 0.86; 95% CI, 0.62-1.21; *P* = .40) (Table 3). In addition, no significant interaction was observed between the mechanical thromboprophylaxis groups and type of prophylactic heparin used (*P* = .08), recent trauma (*P* = .47), or recent surgery (*P* = .07).

Discussion

We found that the use of IPC but not GCS was associated with a significantly decreased risk of incident VTE. This effect was consistent whether the patient was receiving concomitant prophylactic UFH or enoxaparin and whether the admission was related to trauma or surgery.

Table 2—*Number of Incident VTE Events According to Mechanical Thromboprophylaxis Used*

Occurrence of VTE	IPC (n = 229)	GCS (n = 180)	No Mechanical Thromboprophylaxis (n = 389)
Yes	11 (4.8)	18 (10.0)	28 (7.2)
No	218 (95.2)	162 (90.0)	361 (92.8)

Data are presented as No. (%). See Table 1 legend for expansion of abbreviations.

The effectiveness of IPC and GCS in preventing VTE has not been evaluated in RCTs in medical-surgical patients in the ICU[1] as reflected in two systematic reviews.[10,26] A systematic review by the Clinical Guidelines Committee of the ACP evaluated mechanical thromboprophylaxis as a group (GCS and IPC) in hospitalized nonsurgical patients.[27] The review included three trials[28-30] of which two studied GCS and one IPC. The results were influenced mainly by the largest trial, which used GCS and found no significant difference in risk for mortality, symptomatic DVT, or PE but did report an increased risk for lower-extremity skin damage compared with no thromboprophylaxis.[30] Another systematic review by Limpus et al[10] included two RCTs that compared IPC to low-molecular-weight heparin (LMWH) in patients with critical illness related to trauma[11,31] and found IPC to be less effective. As such, the ACP clinical practice guidelines recommend that IPC use be reserved for patients with a contraindication to pharmacologic thromboprophylaxis.[8] Systematic reviews and clinical practice guidelines[3,16,17] combined IPC and GCS together in their meta-analyses and recommendations. The present study demonstrates that the effect of these two modalities on VTE is different and possibly opposing. Therefore, the two modalities should be analyzed and reported separately.

IPC is a mechanical method of delivering compression to the lower extremities.[32] The thromboprophylaxis effect is believed to be related to enhanced venous blood flow in the legs, increase in endogenous fibrinolysis, stimulation of vascular endothelial cells, and reduction in the caliber of veins.[32] Previous studies of IPC effectiveness yielded inconsistent findings. Existing studies have limitations related to sample size and study design. Additionally, the two existing RCTs were conducted in patients with trauma and used LMWH as a comparator.[11,31] Such a comparison has little relevance at present because current clinical practice guidelines recommend pharmacologic thromboprophylaxis as the first choice. The present study demonstrates lower incident VTE with the use of IPC. This association was consistent regardless of the use and type of prophylactic heparin and the type of admission being trauma or surgical related. These findings suggest that the association of lower VTE risk with the use of IPC is not only significant if used as an alternative to UFH or enoxaparin but also significant if used as an adjunct to pharmacologic thromboprophylaxis. Considering the significantly lower risk observed with IPC (aHR, 0.45; 95% CI, 0.22-0.95), the combined strategy of pharmacologic thromboprophylaxis with IPC may be optimal in medical-surgical patients in the ICU.

The use of GCS in critically ill patients is common.[13] GCS is believed to work by reducing the cross-sectional area of the veins and, thus, increasing blood velocity.[33]

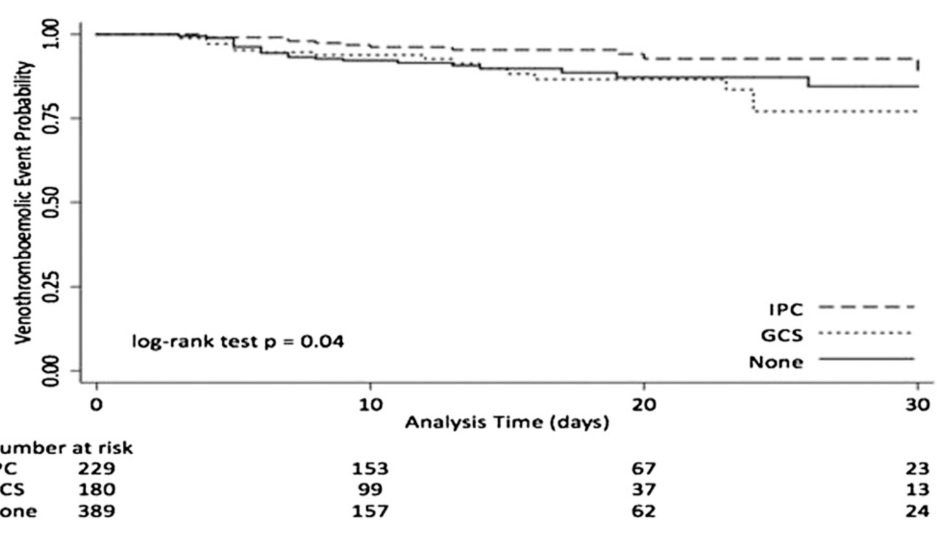

Figure 2. Kaplan-Meier curves for VTE probabilities of the three categories of mechanical devices. See Figure 1 legend for expansion of abbreviations.

Table 3—*Association of IPC and GCS Use With Outcomes*

	Crude Estimates		Propensity Score Adjusted Estimates	
Outcome	HR (95% CI)	*P* Value	aHR (95% CI)	*P* Value
VTE				
IPC	0.48 (0.24-0.97)	.04	0.45 (0.22-0.95)	.03
GCS	1.15 (0.64-2.08)	.64	1.04 (0.59-2.04)	.76
Hospital mortality				
IPC	0.84 (0.63-1.11)	.22	0.92 (0.68-1.24)	.59
GCS	0.75 (0.54-1.03)	.07	0.86 (0.62-1.21)	.40

Comparisons are made with the no mechanical device group as the reference group. aHR = adjusted hazard ratio; HR = hazard ratio. See Table 1 legend for expansion of other abbreviations.

The present study demonstrates that GCS was not associated with lower VTE risk. The findings are consistent with previous evidence showing no reduction of VTE with GCS.[30] In the Clots in Legs or Stockings after Stroke (CLOTS) I trial, 2,518 hospitalized patients with stroke were randomized to thigh-length GCS or to avoidance of GCS. GCS resulted in a nonsignificant difference in DVT risk of 0.5% (95% CI, −1.9% to 2.9%) but with increased skin complications (OR, 4.18; 95% CI, 2.40-7.27). In the CLOTS II trial, 3,114 hospitalized patients with stroke were randomized to thigh-length or below-knee stockings. DVT occurred less frequently with thigh-length stockings than with below-knee stockings (absolute difference, 2.5 percentage points; 95% CI, 0.7-4.4 percentage points; $P = .008$), which is an odds reduction of 31% (95% CI, 9%-47%). Skin breakdown rates were not different between the two groups. The two CLOTS trials suggested that thigh-length stockings do not reduce the risk of DVT in patients with stroke and that use of below-knee stockings is associated with a higher risk for DVT. The findings of the present study in critically ill patients in whom GCS were predominantly below knee were in line with those of the CLOTS I and II trials. However, whether thigh-length GCS in critically ill patients reduce VTE risk remains unclear. Of note, other studies reported decreased risk for DVT in surgical patients and long-distance travelers with the use of below-knee GCS. This differential effect by patient population may be related to differences in the baseline risk of DVT and severity of illness and needs to be explored further. Furthermore, in light of the present findings, the use of GCS, especially below-knee stockings, in critically ill patients needs to be reconsidered.

The interpretation of different studies on mechanical thromboprophylaxis should take into consideration the effect of context. Our hospital launched an institution-wide thromboprophylaxis campaign with implementation of clinical practice guidelines that recommend pharmacologic thromboprophylaxis as the primary mode of therapy. This campaign explains the fact that around 80% of the patients in our study were receiving both mechanical and pharmacologic thromboprophylaxis. This high rate of pharmacologic prophylaxis contrasts, for example, with the CLOTS I and II trials, in which the concomitant use of prophylactic UFH or LMWH during the study period was documented in around 12% to 14% of patients who were not receiving therapeutic anticoagulation. The higher use of pharmacologic thromboprophylaxis seen in the present study is likely to reduce the baseline risk of VTE and may underestimate the potential benefit of IPC or GCS.

The effectiveness of mechanical therapeutic interventions such as IPC or GCS is best examined in RCTs because they provide the best assurance that the observed differences in outcomes are unlikely to be related to confounders. Propensity scores in observational studies have been used to adjust for imbalances in baseline differences. Because investigators have no control over treatment assignment, the differences in the observed covariates between treated and control groups may explain all or part of the observed differences in the outcome and, in turn, may avoid biased estimates of treatment effect. The propensity score attempts to reduce biased estimates of treatment effect by balancing the observed effect of the covariates in the two groups through summarizing their effects in one or more variables and is a more practical method than matching on several covariates, which may not always be possible.

The present study should be interpreted in terms of its strengths and limitations. Its clinical relevance stems from reflecting real-life practice. The VTE rate is consistent with other studies.[2,7] The diagnostic approach for VTE is consistent with standard practice, being based on clinical suspicion rather than on surveillance. Although this approach might be less sensitive than the surveillance-based approach,[2] it is more specific and clinically applicable in medical practice.[34] Other strengths are the prospective inclusion of patients and the use of multiple propensity scores. To our knowledge, this study is the first to specifically address the impact of mechanical devices on VTE risk among medical-surgical patients in the ICU, and the results may be generalizable to a wider population. In terms of limitations, the study was not an RCT; as such, the findings only highlight associations, and cause-and-effect relationships cannot be inferred. However, the various comparison groups were generally comparable, as confirmed by the propensity score analysis. Additionally, given the possible effect of unknown confounders and other issues attendant to an observational study, the observed treatment effect might be larger than the true effect.

Conclusions

In this single-center observational study of 1.5 years duration, we found that the use of IPC was associated with a lower risk of incident VTE, irrespective of concurrent administration of prophylactic UFH or enoxaparin. Furthermore, this association was not specific to admission category. On the other hand, the use of GCS was not associated with lower VTE risk. The study suggests that IPC may have an additive protective effect to pharmacologic thromboprophylaxis in critically ill medical-surgical patients.

Acknowledgments

Author contributions: Dr Arabi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Dr Arabi: contributed to the study conception and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and supervision and final approval of the version to be published.
Dr Khedr: contributed to the analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
Dr Dara: contributed to the analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
Dr Dhar: contributed to the analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
Dr Bhat: contributed to the acquisition of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
Dr Tamim: contributed to the analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
Ms Afesh: contributed to the acquisition of data, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
Financial/nonfinancial disclosures: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Role of sponsors: The unrestricted grant was used to support data collection and management.

References

1. Cook DJ, Crowther MA. Thromboprophylaxis in the intensive care unit: focus on medical-surgical patients. *Crit Care Med*. 2010;38(2)(suppl):S76-S82.
2. Cook D, Crowther M, Meade M, et al. Deep venous thrombosis in medical-surgical critically ill patients: prevalence, incidence, and risk factors. *Crit Care Med*. 2005;33(7):1565-1571.
3. Kahn SR, Lim W, Dunn AS, et al; American College of Chest Physicians. Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2)(suppl):e195S-e226S.
4. National Quality Forum. National voluntary consensus standards for prevention and care of venous thromboembolism: additional performance measures. National Quality Forum website. http://www.qualityforum.org/Publications/2008/10/National_Voluntary_Consensus_Standards_for_Prevention_and_Care_of_Venous_Thromboembolism__Additional_Performance_Measures.aspx. Published October 2008. Accessed February 5, 2012.
5. Agency for Healthcare Research and Quality. Preventing hospital-acquired venous thromboembolism. Appendix A: talking points to attract administration support for venous thromboembolism prevention programs. Agency for Healthcare Research and Quality website. http://www.ahrq.gov/qual/vtguide/vtguideapa.htm. Accessed February 4, 2012.
6. Centers for Medicare & Medicaid Services. Hospital-acquired conditions (present on admission indicator). Centers for Medicare & Medicaid Services website. http://www.cms.hhs.gov/HospitalAcqCond/06_Hospital-Acquired_Conditions.asp. Updated December 8, 2010. Accessed February 4, 2012.
7. Cook D, Meade M, Guyatt G, et al; PROTECT Investigators for the Canadian Critical Care Trials Group and the Australian and New Zealand Intensive Care Society Clinical Trials Group. Dalteparin versus unfractionated heparin in critically ill patients. *N Engl J Med*. 2011;364(14):1305-1314.
8. Qaseem A, Chou R, Humphrey LL, Starkey M, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Venous thromboembolism prophylaxis in hospitalized patients: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2011;155(9):625-632.
9. Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schuünemann HJ; American College of Chest Physicians. Executive summary: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2)(suppl):7S-47S.
10. Limpus A, Chaboyer W, McDonald E, Thalib L. Mechanical thromboprophylaxis in critically ill patients: a systematic review and meta-analysis. *Am J Crit Care*. 2006;15(4):402-410.
11. Kurtoglu M, Yanar H, Bilsel Y, et al. Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin. *World J Surg*. 2004;28(8):807-811.
12. Cook D, Laporta D, Skrobik Y, et al; Canadian ICU Directors Group. Prevention of venous thromboembolism in critically ill surgery patients: a cross-sectional study. *J Crit Care*. 2001;16(4):161-166.
13. Lacherade JC, Cook D, Heyland D, Chrusch C, Brochard L, Brun-Buisson C; French and Canadian ICU Directors Groups. Prevention of venous thromboembolism in critically ill medical patients: a Franco-Canadian cross-sectional study. *J Crit Care*. 2003;18(4):228-237.
14. Müllges W, Steinke E, Moldenhauer G, Berens N. Customary use of compression stockings for prevention of thrombosis in medical intensive care units in Germany [in German]. *Dtsch Med Wochenschr*. 2001;126(31-32):867-871.
15. Limpus A, Chaboyer W. The use of graduated compression stockings in Australian intensive care units: a national audit. *Aust Crit Care*. 2003;16(2):53-58.
16. Geerts WH, Bergqvist D, Pineo GF, et al; American College of Chest Physicians. Prevention of venous thromboembolism:

American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest*. 2008;133(6)(suppl):381S-453S.
17. Gould MK, Garcia DA, Wren SM, et al; American College of Chest Physicians. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2)(suppl):e227S-e277S.
18. Falck-Ytter Y, Francis CW, Johanson NA, et al; American College of Chest Physicians. Prevention of VTE in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2)(suppl):e278S-e325S.
19. Arabi Y, Alshimemeri A, Taher S. Weekend and weeknight admissions have the same outcome of weekday admissions to an intensive care unit with onsite intensivist coverage. *Crit Care Med*. 2006;34(3):605-611.
20. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest*. 2004;126(3)(suppl):338S-400S.
21. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.
22. Spreeuwenberg MD, Bartak A, Croon MA, et al. The multiple propensity score as control for bias in the comparison of more than two treatment arms: an introduction from a case study in mental health. *Med Care*. 2010;48(2):166-174.
23. Brookhart MA, Schneeweiss S, Rothman KJ, Glynn RJ, Avorn J, Stürmer T. Variable selection for propensity score models. *Am J Epidemiol*. 2006;163(12):1149-1156.
24. Hausman JA, McFadden DL. Specification tests for the multinomial logit model. *Econometrica*. 1984;52(5):1219-1240.
25. Fagerland MW, Hosmer DW. A generalized Hosmer-Lemeshow goodness-of-fit test for multinomial logistic regression models. *Stata J*. 2012;12(3):447-453.
26. Segal JB, Streiff MB, Hofmann LV, Thornton K, Bass EB. Management of venous thromboembolism: a systematic review for a practice guideline [published correction appears in *Ann Intern Med*. 2007;146(5):396]. *Ann Intern Med*. 2007;146(3):211-222.
27. Lederle FA, Zylla D, MacDonald R, Wilt TJ. Venous thromboembolism prophylaxis in hospitalized medical patients and those with stroke: a background review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med*. 2011;155(9):602-615.
28. Prasad BK, Banerjee AK, Howard H. Incidence of deep vein thrombosis and the effect of pneumatic compression of the calf in elderly hemiplegics. *Age Ageing*. 1982;11(1):42-44.
29. Muir KW, Watt A, Baxter G, Grosset DG, Lees KR. Randomized trial of graded compression stockings for prevention of deep-vein thrombosis after acute stroke. *QJM*. 2000;93(6):359-364.
30. Dennis M, Sandercock PA, Reid J, et al; CLOTS Trials Collaboration. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet*. 2009;373(9679):1958-1965.
31. Ginzburg E, Cohn SM, Lopez J, Jackowski J, Brown M, Hameed SM; Miami Deep Vein Thrombosis Study Group. Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma. *Br J Surg*. 2003;90(11):1338-1344.
32. Kurtoğlu M, Güloğlu R, Ertekin C, Taviloğlu K, Alimoğlu O. Intermittent pneumatic compression in the prevention of venous thromboembolism in high-risk trauma and surgical ICU patients. *Ulus Travma Acil Cerrahi Derg*. 2005;11(1):38-42.
33. CLOTS (Clots in Legs Or sTockings after Stroke) Trial Collaboration. Thigh-length versus below-knee stockings for deep venous thrombosis prophylaxis after stroke: a randomized trial. *Ann Intern Med*. 2010;153(9):553-562.
34. Sud S, Mittmann N, Cook DJ, et al; Canadian Critical Care Trials Group; E-PROTECT Investigators. Screening and prevention of venous thromboembolism in critically ill patients: a decision analysis and economic evaluation. *Am J Respir Crit Care Med*. 2011;184(11):1289-1298.