Active Ankle Movements Prevent Formation of Lower-Extremity Deep Venous Thrombosis After Orthopedic Surgery

Ye Li, Xiang-Hong Guan, Rui Wang, Bin Li, Bo Ning, Wei Su, Tao Sun, Hong-Yan Li

Corresponding Author: Wei Su, e-mail: suwei_swsw@126.com
Source of support: Departmental sources

Background: The aim of this study was to assess the preventive value of active ankle movements in the formation of lower-extremity deep venous thrombosis (DVT), attempting to develop a new method for rehabilitation nursing after orthopedic surgery.

Material/Methods: We randomly assigned 193 patients undergoing orthopedic surgery in the lower limbs into a case group (n=96) and a control group (n=97). The control group received routine nursing while the case group performed active ankle movements in addition to receiving routine nursing. Maximum venous outflow (MVO), maximum venous capacity (MVC), and blood rheology were measured and the incidence of DVT was recorded.

Results: On the 11th and 14th days of the experiment, the case group had significantly higher MVO and MVC than the control group (all P<0.05). The whole-blood viscosity at high shear rate and the plasma viscosity were significantly lower in the case group than in the control group on the 14th day (both P<0.05). During the experiment, a significantly higher overall DVT incidence was recorded in the control group (8 with asymptomatic DVT) compared with the case group (1 with asymptomatic DVT) (P=0.034). During follow-up, the case group presented a significantly lower DVT incidence (1 with symptomatic DVT and 4 with asymptomatic DVT) than in the control group (5 with symptomatic DVT and 10 with asymptomatic DVT) (P=0.031).

Conclusions: Through increasing MVO and MVC and reducing blood rheology, active ankle movements may prevent the formation of lower-extremity DVT after orthopedic surgery.

MeSH Keywords: Orthopedics • Rehabilitation Nursing • Venous Thrombosis

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/896911
Background

Venous thromboembolism, including deep vein thrombosis (DVT), has long been recognized as the most frequent complication within 7 to 14 days after orthopedic surgery, especially total joint arthroplasty [1]. Without prophylactic therapy, the incidence of DVT and pulmonary embolism reaches up to 60% following orthopedic surgery [2]. The possible damage to the vessel wall during the operation, the venous stasis caused by long-term bed rest, and the hypercoagulability of the blood after the surgery are the 3 main reasons for the formation of DVT [3]. In most cases, the thrombi resolve spontaneously; however, some of them (about 1–4%) may develop into symptomatic and even fatal DVT [4]. Due to fear of the formation of DVT after orthopedic surgery, some patients even refuse to receive orthopedic surgery, which could be the best solution for their diseases [5]. Therefore, a preventive approach to reduce the incidence of postoperative DVT is of great importance.

After orthopedic surgery, doctors usually give 2 kinds of antithrombotic therapies: mechanical thromboprophylaxis and pharmacological thromboprophylaxis [6]. However, the benefit of the above-mentioned methods is impaired by the high cost of mechanical thromboprophylaxis and the adverse effects of pharmacological thromboprophylaxis [7]. In this context, further research is needed. When people walk, there are 4 impulse-aspiration pumps synchronously working: foot pump, leg pump, popliteal pump, and thigh pump [8]. Because they are both related to the calf muscle, the leg pump and the popliteal pump are collectively referred to as the calf muscle pump (CMP), which is the most important pump in the lower limb [9]. It has been suggested that deficient calf muscle function (CMPV) is a causative factor in chronic venous diseases [10]. In addition, ankle joint movement is integral to the activation of the CMP [11]. Taken together, these facts suggest that, for patients without ankle trauma, active ankle movement is a cost-effective approach to activate the CMP in the lower limb and thus reduce the risk of DVT after orthopedic surgery.

In the present study we investigated the effect of active ankle movement in the prevention of DVT in the lower limbs after orthopedic surgery, aiming to reduce financial costs for patients, accelerate postoperative recovery, and improve patient satisfaction.

Material and Methods

Ethic statement

This study was conducted with the approval of the Ethics Committee of Linyi People’s Hospital. All aspects of the study complied with the Declaration of Helsinki [12] and written consent was received from each patient or their families before the examination.

Subjects

In this study, we enrolled 193 patients, who underwent lower-extremity orthopedic surgery in Linyi People’s Hospital between January 2013 and September 2014. Using a random number table, we allocated enrolled patients into either a case group (n=96) or a control group (n=97). Inclusion criteria were: (1) patients who had no history of hip joint replacement, femoral head replacement, or knee joint replacement; (2) patients with no confirmed DVT by color Doppler ultrasonography; and (3) patients who accepted all the required examinations and had no communication obstacles. Exclusion criteria were: (1) patients with combined lower-extremity DVT before the operation; (2) patients with dysemia before the operation; (3) patients with combined hypertension or myocardial infarction; (4) patients with such hemorrhagic diseases as combined cerebrovascular diseases; and (5) patients treated with antithrombotic drug or estrogen a month before the operation.

Routine nursing

Both groups comprised patients who underwent total hip joint replacement, femoral head replacement, or knee joint replacement. All the included patients presented no symptoms or signs of DVT at the end of the operations according to the results of color Doppler ultrasound examination of the lower limbs. The routine post-operation nursing for both groups included: (1) antibiotic injection; (2) X-ray examination for detecting the location of the prosthetic joints before the patients left their bed; (3) instructions for performing joint movements in the unfixed joints and muscle contraction, and massage on the lower limbs; and (4) regular follow-ups, during which patients took antithrombotic drugs, pain-killers, and antibiotics, as required.

Intervention by active ankle movements

In addition to the routine nursing, patients in the case group were required to perform active ankle movements on the first day after the operation. Before the experiment, the attending doctor explained to the patients in the case group the benefits of active ankle movements. After receiving written consent from the patients, the attending doctors gave detailed instructions and helped patients perform active ankle movements. The patients were required to perform active ankle movements in strict accordance with the instructions every day.

Instructions of active ankle movements were: (1) movements should be made in an active way; (2) an ankle movement composed of 20° dorsal flexion, 30° varus, 40° plantar flexion, and 30° valgus flexion in sequence; (3) the ankle movements were
made at a frequency of 30 times/min and at a cycle of 8 min, 1 cycle every 30 min, and 20 cycles each day (during the 1st~14th days after the operation; 7 cycles in the morning, 7 cycles in the afternoon, and 6 cycles in the evening).

The experimental evaluation was conducted by staff blind to the grouping and clinical data of the included patients.

**Measurement of maximum venous outflow (MVO) and maximum venous capacity (MVC)**

The plethysmographic measurements of MVO and MVC were performed on days 1, 2, 5, 7, 9, 11, and 14 postoperative—ly in all patients. Air plethysmography was used to measure MVO and MVC. The patients were asked to lie on their backs, with a 25-cm-thick cushion placed under their heels and their knees bending outward. A 12-cm-wide blood pressure cuff was wrapped around the proximal thigh and another 10-cm-wide blood pressure cuff wrapped around the largest part of the calf. After a brief rest, a 10-cm-wide blood pressure cuff was inflated to reach a pressure of 5.3 kPa (40 mmHg) and then deflated to keep the pressure at 2.0 kPa (15 mmHg), and the polysomnography was conducted at 5 mm/s. At the same time, the 12-cm-wide blood pressure cuff was inflated and reached a pressure of 10 kPa (75 mmHg) and then deflated to keep the pressure at 8.0 kPa (60 mmHg). The rise in the plethysmography curve for the calf was observed. Two to three seconds after the curve reached its highest point, the 12-cm-wide blood pressure cuff was deflated quickly and completely, followed by a rapid decline of the curve. MVC was calculated as the vertical distance from the baseline to the highest point of the curve. MVO was calculated by drawing a vertical line from the point at 3 s after the complete deflation to meet the endpoint of the declining line, and the vertical distance of the starting point to the meeting point was defined as MVO. For each operation, 1 person was specifically assigned to timing and the data were recorded as those presented on the screen.

**Measurement of hemorheology**

A fully-automatic hemorheologic analyzer and paired reagents (F2805C, Chongqing Weiduo Technology Co., Ltd.) were used for recording the hemorheologic changes on days 1 and 14 postoperatively in all patients by measuring the whole-blood viscosity at high and low shear rates, the plasma viscosity, and the fibrinogen concentration.

**Detection of DVT**

During the experiment, all patients were under careful observation. When symptoms and signs of DVT were detected, the patients were given an examination of the lower limbs with color Doppler ultrasound (VIVID7; CE, USA) and then evaluated. The diagnostic criteria for lower-extremity DVT were: (1) patients had a rapid onset accompanied with increasing pain or sharp pain and had pressing pain in the femoral triangle or shank; (2) patients had excessive swelling; (3) patients had a dark red affected limb and had increased body temperature; (4) patients had an affected limb with excessive distension in the superficial vein; and (5) patients had positive Homán’s signs. Postoperative patients with these 5 clinical symptoms and 2 or more DVT signs were highly suspected to have DVT if they did not have acute arterial embolism, acute lymphangitis, erysipelas, injuring hematoma at the shank, or fibrofascitis at the shank. [13].

**Follow-up**

Of the 193 included patients, 184 patients were followed up for 6 months after the experiment, with 93 in the case group and 91 in the control group. In the first month, contacts with the patients were made weekly. If any DVT signs were found, patients were told to make a return visit to the doctors and receive color Doppler ultrasonography on the lower limbs. Those patients with no DVT signs in the first 3 weeks received color Doppler ultrasonography of the lower limbs in the fourth week and were evaluated in terms of their susceptibility to DVT. In the following 5 months, contacts were made at a frequency of once a month. Patients who reported clinical symptoms of DVT at the contact immediately received color Doppler ultrasonography of the lower limbs, while those who did not report clinical symptoms of DVT received color Doppler ultrasonography at the end of each month. The incidence of DVT was recorded.

**Statistical analysis**

Data analyses were conducted with SPSS 18.0 (SPSS Inc., Chicago, IL, USA). The qualitative data were analyzed with the chi-squared test and rank-sum test [14] while the quantitative data were analyzed with repeated measures test [15]. The other data were analyzed using the t test and are presented as mean ± standard deviation. For data following non-normal distribution, the non-parametric Mann-Whitney U test was used [16].

**Results**

**Baseline characteristics**

The case and control groups were highly similar in age, sex distribution, pathological type, anesthesia method, operative site, the use of antithrombotic drug (rivaroxaban and LMWH), vitamins, antibiotics, and analgesics, as well as the duration of out-of-bed exercise and duration of time in bed per day (all P>0.05) (Table 1).
In the first 14 days after the operation, the cases and the controls had increasing MVO levels (case: $F=30.440, P<0.001$; control: $F=18.910, P<0.001$) and showed significant differences on the 11th day and 14th day (11th day: $t=2.217, P=0.028$; 14th day: $t=2.860, P=0.005$) (Table 2).

MVC

An increasing trend in MVC level were identified in both the case group and the control group in the first 14 days after the operation (the case group: $F=94.320, P<0.001$; the control group: $F=52.440, P<0.001$). On the 11th day and 14th days, a significant difference in the MVC levels was found between the case group and the control group (11th day: $t=2.304, P=0.022$; 14th day: $t=3.098, P=0.002$) (Table 3).

Blood rheology

On the first day after the operation, no significant differences between the case group and the control group were identified in whole blood viscosity at both high and low shear rate, plasma viscosity, and fibrinogen concentration (all $P>0.05$). On the 14th day after the operation, cases and controls had significantly lower whole-blood viscosity at low shear rate (cases: $11.87\pm0.87$ vs. $12.29\pm0.78$, controls: $12.07\pm0.62$ vs. $12.34\pm0.69$, both $P<0.05$) and significantly higher expressions of fibrinogen concentration (cases: $2.39\pm0.76$ vs. $2.15\pm0.67$; controls: $2.32\pm0.65$ vs. $2.12\pm0.52$, both $P<0.05$) compared to the first day after the operation. The cases had significantly lower whole-blood viscosity at high shear rate and plasma viscosity than the controls (whole-blood viscosity at high shear: $5.62\pm0.48$ vs. $5.84\pm0.34$; plasma viscosity: $1.91\pm0.18$ vs. $2.01\pm0.18$, both $P<0.05$) (Table 4).

MVO

In the first 14 days after the operation, the cases and the controls had increasing MVO levels (case: $F=30.440, P<0.001$; control: $F=18.910, P<0.001$) and showed significant differences on the 11th day and 14th day (11th day: $t=2.217, P=0.028$; 14th day: $t=2.860, P=0.005$) (Table 2).

### Table 1. The baseline characteristics of the case group and the control group.

|                                | Case group (n=96) | Control group (n=97) | $t$/$\chi^2$ | $P$ |
|--------------------------------|------------------|----------------------|--------------|-----|
| Age (years)                    | 53.6±5.4         | 54.3±6.4             | 0.819        | 0.414 |
| Gender (M/F)                   | 77/19            | 72/24                | 0.749        | 0.387 |
| Disease location               |                  |                      |              |     |
| Left limb                      | 45               | 44                   | 0.263        | 0.877 |
| Right limb                     | 34               | 37                   |              |     |
| Both limbs                     | 17               | 15                   |              |     |
| Anesthesia methods             |                  |                      |              |     |
| General                        | 76               | 73                   | 0.494        | 0.781 |
| Intravertebral                 | 19               | 21                   |              |     |
| Other                          | 1                | 2                    |              |     |
| Surgical site                  |                  |                      |              |     |
| Hip/thigh                      | 65               | 61                   | 0.495        | 0.482 |
| Knee                           | 31               | 36                   |              |     |
| Antithrombotic reagent         |                  |                      |              |     |
| Rivaroxaban                     | 12               | 9                    | 0.516        | 0.472 |
| LMWH                           | 84               | 88                   |              |     |
| Antibiotic (day)               | 4.1±1.1          | 3.9±1.1              | 1.193        | 0.235 |
| Analgesic                      | 47               | 36                   | 0.136        | 0.713 |
| Vitamin                        | 15               | 19                   | 2.088        | 0.149 |
| Exercise off bed per day (min) | 53.3±6.9         | 54.9±6.2             | 1.591        | 0.113 |
| Time of lying in bed           | 10.6±1.2         | 10.9±1.4             | 1.598        | 0.112 |

M – male; F – female; LMWH – low molecular weight heparin.
At the end of the experiment, no patient was diagnosed with symptomatic DVT, and 1 patient in the case group and 8 patients in the control group were diagnosed with asymptomatic DVT. The total incidence of DVT was significantly different between the case group and the control group (1/96 vs. 8/97, \( P = 0.034 \)) (Table 5).

At the end of the follow-up, another 5 cases were diagnosed with DVT (total DVT incidence of 5.3%); 1 with symptomatic DVT (1.0%) and the other 4 with asymptomatic DVT (4.2%). In the control group, 12 more controls were diagnosed with DVT (total DVT incidence of 15.5%); 5 with symptomatic DVT (5.2%) and the other 10 with asymptomatic DVT (10.3%). The difference in the total incidence of DVT was significant between the case group and the control group (5.3% vs. 15.5%, \( P=0.031 \)) (Table 6). As shown in Figure 1, the patients with symptomatic DVT had observable limb swelling and sharp pain and were diagnosed using color Doppler ultrasonography.

### The incidence of DVT at the end of the experiment

At the end of the experiment, no patient was diagnosed with symptomatic DVT, and 1 patient in the case group and 8 patients in the control group were diagnosed with asymptomatic DVT. The total incidence of DVT was significantly different between the case group and the control group (1/96 vs. 8/97, \( P=0.034 \)) (Table 5).

### The incidence of DVT at the end of the follow-up

At the end of the follow-up, another 5 cases were diagnosed with DVT (total DVT incidence of 5.3%); 1 with symptomatic DVT (1.0%) and the other 4 with asymptomatic DVT (4.2%). In the control group, 12 more controls were diagnosed with DVT (total DVT incidence of 15.5%); 5 with symptomatic DVT (5.2%) and the other 10 with asymptomatic DVT (10.3%). The difference in the total incidence of DVT was significant between the case group and the control group (5.3% vs. 15.5%, \( P=0.031 \)) (Table 6). As shown in Figure 1, the patients with symptomatic DVT had observable limb swelling and sharp pain and were diagnosed using color Doppler ultrasonography.

### Discussion

An important reason for developing postoperative DVT is venous stasis or slow venous return in the lower limb caused by prolonged bed rest after orthopedic surgery [17]. In the present study, we recorded MVO, MVC, and the changes of blood flow velocity in the deep veins of the lower limbs.

|                | Control group (n=97) | Case group (n=96) | t    | P   |
|----------------|----------------------|-------------------|------|-----|
| 1st day        | 11.84±2.02           | 12.18±2.13        | 1.135| 0.258|
| 2nd day        | 12.06±2.78           | 12.24±2.27        | 1.398| 0.164|
| 5th day        | 12.57±2.03           | 12.80±2.13        | 0.766| 0.445|
| 7th day        | 12.78±2.17           | 13.10±2.27        | 0.998| 0.319|
| 9th day        | 13.58±2.50           | 14.13±2.18        | 1.625| 0.106|
| 11th day       | 14.08±2.88           | 14.90±2.20*       | 2.217| 0.028|
| 14th day       | 14.27±2.36           | 15.24±2.34*       | 2.86 | 0.005|
| P              | <0.001               | <0.001            |      |     |

* Refers to significant difference (\( P<0.05 \)) between the case group and the control group.

|                | Control group (n=97) | Case group (n=96) | t    | P   |
|----------------|----------------------|-------------------|------|-----|
| 1st day        | 5.47±2.23            | 5.82±1.94         | 1.16 | 0.247|
| 2nd day        | 5.89±2.16            | 6.02±1.06         | 1.083| 0.286|
| 5th day        | 6.40±1.89            | 6.73±1.87         | 1.216| 0.226|
| 7th day        | 6.69±1.90            | 7.08±1.98         | 1.392| 0.165|
| 9th day        | 7.91±2.31            | 8.36±1.87         | 1.484| 0.14 |
| 11th day       | 8.97±3.03            | 9.82±1.97*        | 2.304| 0.022|
| 14th day       | 10.13±2.53           | 11.19±2.20*       | 3.098| 0.002|
| P              | <0.001               | <0.001            |      |     |

* Refers to significant difference (\( P<0.05 \)) between the case group and the control group.
rheology indexes along with DVT incidence after orthopedic surgery, aiming to explore the preventive effect of active ankle movement on the development of DVT.

The normal operation of the lower-extremity venous system relies on the venous valves and a complex system of impulse-aspiration pumps [18]. CMP, the most important pump in the lower limb, is the motive force to return blood to the heart; an inefficient CMP may lead to chronic venous insufficiency [19,20]. Whole-body flexibility and coordination can be improved using the knowledge that the CMP depends on ankle joint mobility and competency of veins, and that active movement has better results in the prevention of DVT than passive movement [21]. Therefore, we believe that active ankle movement can activate the CMP and thus promote vein circulation in the lower limbs and prevent formation of post-operative DVT in patients undergoing lower-extremity orthopedic surgery. In our case-control study we observed significantly higher MVO and MVC and markedly improved blood rheology in the cases on the 14th day than in the controls. Thus, it is safe to conclude that active ankle movement combined intervention has better efficacy than routine nursing

### Table 4. The hemorheological changes in the case group and the control group during the experiment.

|                          | Control group (n=97) | Case group (n=96) |
|--------------------------|----------------------|-------------------|
| Whole blood viscosity at high shear rate (mpas) |                      |                   |
| 1st day                  | 5.95±0.46            | 5.89±0.56         |
| 14th day                 | 5.84±0.34            | 5.62±0.48**       |
| Whole blood viscosity at low shear rate (mpas) |                      |                   |
| 1st day                  | 12.34±0.69           | 12.29±0.78        |
| 14th day                 | 12.07±0.62*          | 11.87±0.87*       |
| Plasma viscosity (mpas)  |                      |                   |
| 1st day                  | 2.05±0.19            | 2.01±0.21         |
| 14th day                 | 2.01±0.18            | 1.91±0.18**       |
| Fibrinogen concentration (mpas) |                      |                   |
| 1st day                  | 2.12±0.52            | 2.15±0.67         |
| 14th day                 | 2.32±0.65*           | 2.39±0.76*        |

* Refers to significant difference (P<0.05) of with-in group comparisons with the values detected on the 1st day *# refers to significant difference (P<0.05) of between group comparisons with the values detected on the same day.

### Table 5. The incidence of DVT during the experiment.

|                          | Patients with symptomatic DVT | Patients with asymptomatic DVT | Total number of DVT | P        |
|--------------------------|-------------------------------|--------------------------------|---------------------|---------|
| Case group (n=96)        | 0 (0.0%)                      | 1 (1.0%)                       | 1 (1.0%)            | 0.034   |
| Control group (n=97)     | 0 (0.0%)                      | 8 (8.2%)                       | 8 (8.2%)            |         |

DVT – deep vein thrombosis.

### Table 6. The incidence of DVT during the follow-up.

|                          | Patients with symptomatic DVT | Patients with asymptomatic DVT | Total number of DVT | P        |
|--------------------------|-------------------------------|--------------------------------|---------------------|---------|
| Case group (n=96)        | 1 (1.0%)                      | 4 (4.2%)                       | 5 (5.3%)            | 0.031   |
| Control group (n=97)     | 5 (5.2%)                      | 10 (10.3%)                     | 15 (15.5%)          |         |

DVT – deep vein thrombosis.
in promoting venous return in the lower limbs and avoiding
vein stasis. Concordantly, Sochart and Hardinge also suggested
that ankle joint movement is an effective way to prevent
post-operative DVT due to its ability to increase venous return
in the lower limbs [22]. A reasonable explanation for this re-
sult is that during ankle joint movements, the calf muscle con-
tracts and compresses the intramuscular and deep veins, rais-
ing venous pressure and propelling blood from the lower limb
toward the heart [23]. Following the raised venous pressure,
MVO and MVC is increased and the blood velocity increases.
In this regard, active ankle movement could be considered as
an effective way to prevent development of DVT.

The recorded incidence of DVT during the experiment and fol-
low-up show that the case group had significantly fewer pa-
tients with asymptomatic DVT and patients with symptomatic
DVT than the control group, suggesting that the active ankle
movement combined intervention has better efficacy in re-
ducing the incidence of post-operative DVT compared to rou-
tine nursing. Consistent with our results, Palamone et al. re-
ported that foot and ankle exercises have a promising role in
reducing DVT incidence in neurological surgery intensive care
patients when these exercises are diligently adhered to [24].
Sa-Ngasoongsong et al. also recommended active ankle mo-
tion to prevent DVT during post-surgery recovery [25].

**Conclusions**

We provided evidence that active ankle movement can pro-
duce higher MVC and MVO and faster blood velocity, possibly
through the activation of the CMP, and it promotes venous
return and vein circulation. We believe that the active ankle
movement combined intervention is effective in preventing
the formation of lower-extremity DVT after orthopedic sur-
gery, accelerating postoperative recovery and improving pa-
tient satisfaction. However, further research with larger sam-
ple sizes is needed to confirm our results.

**Competing interests**

The authors have declared that no competing interests exist.
References:

1. Colwell CW Jr., Froimson MI, Mont MA et al: Thrombosis prevention after total hip arthroplasty: A prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin. J Bone Joint Surg Am, 2010; 92: 527–35

2. Geerts WH, Bergqvist D, Pineo GF et al: Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th ed.). Chest, 2008; 133: 3815–4535

3. Saha P, Humphries J, Modarai B et al: Leukocytes and the natural history of deep vein thrombosis: current concepts and future directions. Arterioscler Thromb Vasc Biol, 2011; 31: 506–12

4. Elkeibloom JW, Karihikeyan G, Fagel N, Hirsh J: American Association of Orthopedic Surgeons and American College of Chest Physicians guidelines for venous thromboembolism prevention in hip and knee arthroplasty differ: what are the implications for clinicians and patients? Chest, 2009; 135: 513–20

5. McHugh GA, Luker KA, Campbell M et al: Pain, physical functioning and quality of life of individuals awaiting total joint replacement: a longitudinal study. J Eval Clin Pract, 2008; 14: 19–26

6. Bozzato S, Galli L, Ageno W: Thromboprophylaxis in surgical and medical patients. Semin Respir Crit Care Med, 2012; 33: 163–75

7. Solayar GN, Shannon Fl: Thromboprophylaxis and orthopaedic surgery: options and current guidelines. Malays J Med Sci, 2014; 21: 71–77

8. Gardner AM, Fox RH: Peripheral venous physiology. In: Gardner AM, Fox RH (eds.) The return of the blood to the heart. London: John Libbey, 1993; 61–87

9. Hickey BA, Morgan A, Pugh N, Perera A: The effect of lower limb cast immobilization on calf muscle pump function: a simple strategy of exercises can maintain flow. Foot Ankle Int, 2014; 35: 829–33

10. Yamaki T, Nozaki M, Sakurai H et al: Advanced chronic venous insufficiency is associated with increased calf muscle deoxygenation. Eur J Vasc Endovasc Surg, 2010; 39: 787–94

11. Dix FP, Brooke K, McCollum CN: Venous disease is associated with an impaired range of ankle movement. Eur J Vasc Endovasc Surg, 2003; 25: 556–61

12. MPN: World Medical Association publishes the Revised Declaration of Helsinki. Natl Med J India, 2014; 27: 56

13. LV HS: Deep veinous thrombosis following artificial joint replacement. Chinese Journal of Orthopaedics, 1999; 19: 155–60

14. Saini V, McClure JT, Leger D et al: Antimicrobial use on Canadian dairy farms. J Dairy Sci, 2011; 95: 1209–21

15. Minahan C, Sheehan B, Detreband R et al: Repeated-sprint cycling does not induce respiratory muscle fatigue in adult animals: measurements from the powerbreath(R) inspiratory muscle trainer. J Sports Sci Med, 2015; 14: 233–38

16. Tulek F, Kahraman A, Taskin S et al: Determination of risk factors and perinatal outcomes of singleton pregnancies complicated by isolated single umbilical artery in Turkish population. J Turk Ger Gynecol Assoc, 2015; 21: 21–24

17. Rostagno C: Prophylaxis of venous thromboembolism in major orthopedic surgery: A practical approach. Cardiovasc Hematol Agents Med Chem, 2013; 11: 230–42

18. Ulh JF, Gillet C: Anatomy of the veno-muscular pumps of the lower limb. Phlebology, 2015; 30: 180–93

19. Robertson L, Lee Al, Gallagher K et al: Risk factors for chronic ulceration in patients with varicose veins: a case control study. J Vasc Surg, 2009; 49: 1490–98

20. Reck C: Calf pump activity influencing venous hemodynamics in the lower extremity. Int J Angiol, 2013; 22: 1490–98

21. Staubesand J, Heisterkamp T, Stege H: Use of duplex sonography to investigate the effect of active and passive movement at the ankle joint for promoting venous return. Clin Anat, 1995; 8: 96–101

22. Sochard DH, Hardinge K: The relationship of foot and ankle movements to venous return in the lower limb. J Bone Joint Surg Br, 1999; 81: 700–4

23. Meissner MH, Moneta G, Burnand K et al: The hemodynamics and diagnosis of venous disease. J Vasc Surg, 2007; 46(Suppl S): 1490–245

24. Palamone J, Brossny V, Groth M, Morris L, Kwasny M: "Tap and twist": preventing deep vein thrombosis in neuroscience patients through foot and ankle range-of-motion exercises. J Neurosci Nurs, 2011; 43: 308–14; quiz 315–6

25. Sa-Ngasoongsong P, Channoom T, Kawinwonggowit V et al: Postoperative blood loss reduction in computer-assisted surgery total knee replacement by low dose intra-articular tranexamic acid injection together with 2-hour clamp drain: a prospective triple-blinded randomized controlled trial. Orthop Rev, 2011; 3: e12