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Full Length Article

Effects of forced deep breathing on blood flow velocity in the femoral vein: Developing a new physical prophylaxis for deep vein thrombosis in patients with plaster cast immobilization of the lower limb

Keisuke Nakanishi[a], Naonobu Takahira[a,b,c,*], Miki Sakamoto[c], Minako Yamaoka-Tojo[c], Masato Katagiri[d], Jun Kitagawa[a]

[a] Sensory and Motor Control, Functional Restoration Sciences, Kitasato University Graduate School of Medical Sciences, 1-15-1, Kitasato, Minami-ku, Sagamihara-shi, Kanagawa 252-0373, Japan
[b] Department of Orthopaedic Surgery, Kitasato University Graduate School of Medical Sciences, 1-15-1 Kitasato, Minami-ku, Sagamihara-shi, Kanagawa 252-0373, Japan
[c] Physical Therapy Course, Department of Rehabilitation, Kitasato University School of Allied Health Sciences, 1-15-1 Kitasato, Minami-ku, Sagamihara-shi, Kanagawa 252-0373, Japan
[d] Department of Medical Laboratory, Kitasato University School of Allied Health Sciences, 1-15-1, Kitasato, Minami-ku, Sagamihara-shi, Kanagawa 252-0373, Japan

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ABSTRACT

Introduction: Patients with plaster cast immobilization of the lower limb have an estimated symptomatic venous thromboembolism rate of 5.5%. However, there is currently no practical physical prophylaxis for deep-vein thrombosis (DVT). The objective of this study was to examine the effects of forced deep breathing on peak blood velocity in the superficial femoral vein (PBVFV), which is a surrogate measure of the efficacy of thromboprophylaxis against DVT, in patients with plaster cast immobilization of the lower limb.
Materials and methods: Nine young males and 18 elderly males were recruited. We immobilized the right lower limb of each subject with a plaster splint and measured PBVFV during forced deep breathing in supine and sitting positions.
Results: In all subjects, PBVFV during forced deep breathing in both positions was significantly higher than at rest. There was no significant difference in the PBVFV change ratio for three breathing rates in the sitting position for the young subjects (15 breaths/min: 415%, 5 breaths/min: 475%, 3 breaths/min: 483%), whereas that for the elderly subjects at 3 breaths/min (449%) was significantly higher than that at 15 breaths/min (284%).
Conclusions: Forced deep breathing significantly increased PBVFV in patients with plaster cast immobilization of the lower limb in both supine and sitting positions. Testing the efficacy and adherence in clinical contexts, and following up with the incidence rate of DVT in future studies, is necessary for the development of a new physical prophylaxis for DVT.

1. Introduction

The incidence rate of a first venous thromboembolism (VTE), i.e., deep vein thrombosis (DVT) and pulmonary embolism (PE), is 1–2 per 1000 person-years in the general population, and increases with age (up to 1% per year) in the elderly [1–5]. The mortality rate of VTE is high, and is estimated at 1.8% in the first month in non-cancer patients with a DVT and 6.8% in non-cancer patients with a pulmonary thromboembolism (PTE) [1]. The high risk of VTE in patients undergoing orthopedic surgery is well documented; plaster cast immobilization in particular is linked with an increased risk of symptomatic VTE, and lower limb immobilization specifically is associated with a 73-fold increased risk of VTE [6]. The most recent meta-analyses and reviews in patients with plaster cast immobilization of the lower limb, involving 1456 patients [7] and 1490 patients [8], show that VTE incidence approaches 20% without prophylaxis. Evidence from randomized

Abbreviations: ACCP, American College of Chest Physicians; BMI, body mass index; DVT, deep vein thrombosis; ICC, intraclass correlation coefficients; IPC, intermittent pneumatic compression; PBV, peak blood velocity; PBVFV, peak blood velocity in the superficial femoral vein; VTE, venous thromboembolism

* Corresponding author at: Department of Rehabilitation, Kitasato University School of Allied Health Sciences, 1-15-1, Kitasato, Minami-ku, Sagamihara-shi, Kanagawa 252-0374, Japan.
E-mail addresses: takahira@med.kitasato-u.ac.jp (N. Takahira), mikis@kitasato-u.ac.jp (M. Sakamoto), myamaoka@med.kitasato-u.ac.jp (M. Yamaoka-Tojo), mkata@kitasato-u.ac.jp (M. Katagiri), kitagawa@kitasato-u.ac.jp (J. Kitagawa).

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controlled trials shows that the use of low-molecular-weight heparin leads to a decrease in the mean VTE incidence rate (17.1% to 9.6%) during plaster cast immobilization [7]. However, compared to the extensive trials on major joint replacement or hip fracture surgery, there is a paucity of studies on the use of thromboprophylaxis in patients with lower limb plaster cast immobilization, and the risk of VTE in these patients is not sufficient to justify the use of anticoagulant prophylaxis, since the risk of bleeding is considerable (0.3% major bleeding) [8,9]. Therefore, the 9th American College of Chest Physicians (ACCP) guidelines suggest that the benefit of pharmacological thromboprophylaxis in patients with isolated lower leg injuries requiring leg immobilization is unclear. Also, the patient population was quite heterogeneous, patients with a higher risk for VTE were excluded, and detailed information with regard to immobility was not provided [9]. Further, the latest randomized controlled trial (POT-CAST trial) shows that prophylaxis with low-molecular-weight heparin for immobilization due to casting was not effective for the prevention of symptomatic venous thromboembolism [10]. Developing a highly cost-effective prophylaxis for VTE to replace pharmacological prophylaxis is therefore an urgent priority for patients with plaster cast immobilization of the lower limb.

Physical DVT prophylaxis eliminates serious complications such as bleeding, and is currently receiving considerable attention. For instance, the 9th ACCP guidelines recommend the use of intermittent pneumatic compression (IPC) to prevent DVT in patients undergoing total hip arthroplasty, total knee arthroplasty, or hip fracture surgery [9]. The application of IPC therapy to patients undergoing lower limb plaster cast immobilization for ruptured Achilles tendons reduced the incidence of DVT at two weeks post-operatively, but not at six weeks post-operatively [11]. In addition, it has been hypothesized that adjuvant IPC beneath an orthotic would reduce the risk of DVT during lower limb post-operative immobilization, but such treatment cannot be recommended due to the high DVT incidence rate associated with malfunctioning IPC devices [12]. Indeed, the application of an IPC device to a lower limb beneath a plaster cast in patients with ruptured Achilles tendons or ankle fractures was associated with high rates (50%) of adverse events (e.g., skin ulceration or maceration), in addition to inconclusive evidence for VTE prevention [13]. Therefore, the benefits of IPC therapy beneath a plaster cast are unclear. In a previous study, we applied an IPC device to the thigh of subjects with below-knee plaster cast immobilization, and achieved a significant increase in peak blood velocity (PBV) in the superficial femoral vein and the popliteal vein [14]. However, this method is not applicable for patients with above-knee plaster casts. In summary, there is currently no practical physical prophylaxis for DVT in patients with plaster cast immobilization of the lower limb.

We thus considered taking advantage of the respiratory muscle pump, which, along with the skeletal muscle pump, is widely acknowledged as a powerful mechanism for accelerating venous return from the lower limb. For example, it has been suggested that marked increases in PBV in the femoral vein occur throughout a predominantly ribcage inspiration [15,16], and non-forced deep breathing in a supine position results in a 1.5-fold increase in PBV in healthy young males [20]. Lower limb PBV is considered a surrogate measure of prophylactic effects against thrombosis, because the use of IPC devices that especially affect PBV is associated with a significantly lower rate of VTE [18,19]. Although deep breathing may be a useful prophylactic for DVT, its preventive effects are probably minimal, because the increase in PBV achieved is lower than that generated by IPC or ankle exercise [14,20,21]. On the other hand, increased respiratory muscle excursion can augment the pressure changes in the intrahepatic inferior vena cava [22], and therefore enhance respiratory modulation of the femoral venous return [23]. In addition, the respiratory collapse of the inferior vena cava during slow respiration with inspiratory pause was greater than that in normal respiration [24]. From the above, we understand that venous return is affected by respiratory patterns (respiratory muscle pressure, respiratory rate, and breath holding), and that forced deep breathing effectively augments PBV in the lower limb.

The objective of this study was to examine the effects of forced deep breathing on PBV in the superficial femoral vein (PBVFV), which is a surrogate measure of thromboprophylaxis efficacy, and to consider forced deep breathing as a physical prophylaxis for DVT in patients with plaster cast immobilization of the lower limb.

2. Materials and methods

2.1. Study participants and characteristics

This study was approved by the Ethics Committee of the Kitasato University School of Medicine (no. 2013–004). We recruited nine young healthy male volunteers and 18 elderly male volunteers, none of whom had a medical history, but who were registered with silver human resource centers. Based on the World Health Organization and the Ministry of Health, Labour and Welfare, we defined people aged 65 or above as “elderly”, and aged 15 to 24 as “young”. We recorded age, height, body weight, body mass index (BMI), Brinkman index (a measure of cigarette use) [25], and medications for all subjects, and all eligible subjects provided written informed consent before inclusion in the trial. Exclusion criteria included any of the following conditions: thrombophlebitis, arteriosclerosis obliterans, any thromboembolic event, malignant tumors, lower limb or pelvic bone fractures, sensory disturbances, inflammatory diseases, swelling, necrosis, epidermization, cerebrovascular disorders, heart failure, respiratory illness, kidney failure, systolic blood pressure above 180 mm Hg, and a history of diastolic blood pressure above 110 mm Hg.

2.2. Study procedure and measurements with Doppler ultrasound

Subjects were advised to avoid strenuous exercise, such as jogging, and to consume liquids as usual on the day of the test. Each subject changed into shorts in the examination room, and we then immobilized his right lower leg and ankle with a plaster splint. The subjects were instructed to relax and to avoid talking loudly, falling asleep, and contracting body muscles as much as possible during the protocol. PBVFV was measured in the supine and sitting positions, using pulsed Doppler ultrasound with a 7.5-MHz linear probe interfaced with an ultrasound unit (Pro Sound SSD-4000, ALOKA, Inc., Wallingford, United States of America). The PBVFV was measured from the anterior side, approximately 3 cm distal to the deep femoral vein junction. The Doppler angle of the superficial femoral vein was maintained at $< 60°$. First, PBVFV was measured in triplicate with the subjects at rest in the supine position. Next, we measured PBVFV in duplicate during forced deep breathing, starting with the fastest breathing rate and progressively slowing down (15, then 5, then 3 breaths/min) (Fig. 1A). The mean values obtained from these measurements were used in the analysis. The subjects then sat on a chair, with thighs parallel to the floor and knees bent at 60 degrees, and the same protocol was used to measure PBVFV. We ensured that the subjects sat far enough forward to avoid compressing the superficial femoral vein. All measurements were taken by the same skilled tester. Prior to the primary experiment, we confirmed the intraclass correlation coefficients (ICC) of the blood flow measurements in a preliminary experiment, and obtained confirmed excellent measurement accuracy [ICC (1, 1) = 0.86; ICC (1, 3) = 0.95]. We removed the plaster splint immediately after completing the measurements; this process took approximately 1.5 h. The subjects also practiced forced deep breathing before the measurements were taken, and we confirmed that they experienced no dizziness or respiratory discomfort as a result of the deep breathing. A physical therapist was present to monitor the condition of the subjects and manage risks during the experiment.