암재활

게시일시 및 장소 : 10 월 18 일(금) 08:30-12:20 Room G(3F)

질의응답 일시 및 장소 : 10 월 18 일(금) 10:00-10:45 Room G(3F)

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Two Different Ways of Extracorporeal Shock Wave Therapy in a Rat Model of Secondary Lymphedema

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Background

Lymphedema is a clinically incurable disease that occurs commonly after lymph node dissection and/or radiation. Several studies have recently demonstrated that low-energy extracorporeal shock wave therapy (ESWT) could promote vascular endothelial growth factor (VEGF) and lymphangiogenesis. Although low-energy ESWT is suggested to be therapeutic strategy for lymphedema, its effective methodologic approach is unclear. We thus studied the effectiveness of two different ESWT methods on lymph node dissection induced secondary lymphedema.

Methods

A rat forelimb model of lymphedema was created by right axillary lymph node dissection. Ten days after surgery, 17 Sprague-Dawley rats were randomly divided into 3 groups; a group that received 500 shots of ESWT only in lymphedematous forelimb (Forelimb/ESWT, n = 5), a group that received 300 shots of ESWT in axilla area as well as 200 shots of ESWT in lymphedematous forelimb (Axilla+Forelimb/ESWT; n = 5), and a lymphedematous limb group (control, n = 7). Low-energy shock waves (0.05 mj/mm2) were applied three times per week for four weeks. Circumferences of wrist and 2.5 cm above wrist were measured 3 days, 7 days, and 10 days after surgery and every 1 week during ESWT application, and 14 days after the last ESWT application. Immunohistochemical staining of pan-endothelial marker (CD31) and lymphatic vessel endothelial hyaluronan receptor-1 (LYVE-1) and western blot analysis of VEGF-C and VEGF receptor 3 (VEGFR3) were performed at 14 days after the last ESWT application.

Results

Circumferences of wrist and 2.5 cm above wrist were decreased at both Forelimb/ESWT and Axilla+Forelimb/ESWT groups compared to control group (Fig. 1). Immunohistochemistry of the rat forelimbs showed that mean (±SD) CD31-positive vessels was 5.7(±0.61) in Axilla+Forelimb/ESWT group, 4.6 (±0.91) in Forelimb/ESWT group, and 4.02(±1.06) in opposite forelimbs that were not induced edema. Mean (±SD)

LYVE-1-positive vessels showed 9.77(±2.02) in Axilla+Forelimb/ESWT group, 9.52(±0.87) in Forelimb/ESWT group, and 8.86(±0.88) in opposite forelimbs that were not induced edema (Fig. 2). Western blot analysis showed that the expression of VEGF-C was 2.83-fold in Axilla+Forelimb/ESWT group, 1.87-fold in Forelimb/ESWT group, and 1.67-fold in in opposite forelimbs that were not induced edema. The expression of VEGFR3 was 2.49-fold in Axilla+Forelimb/ESWT group, 1.53-fold in Forelimb/ESWT group, and 1.27-fold in opposite forelimbs that were not induced edema (Fig. 3).

Conclusion

Our preliminary study suggested that angiogenesis and lymphangiogenesis could be differently induced according to the ways of ESWT application on lymphedema. Further complementary studies involving larger case numbers are warranted to corroborate these findings.

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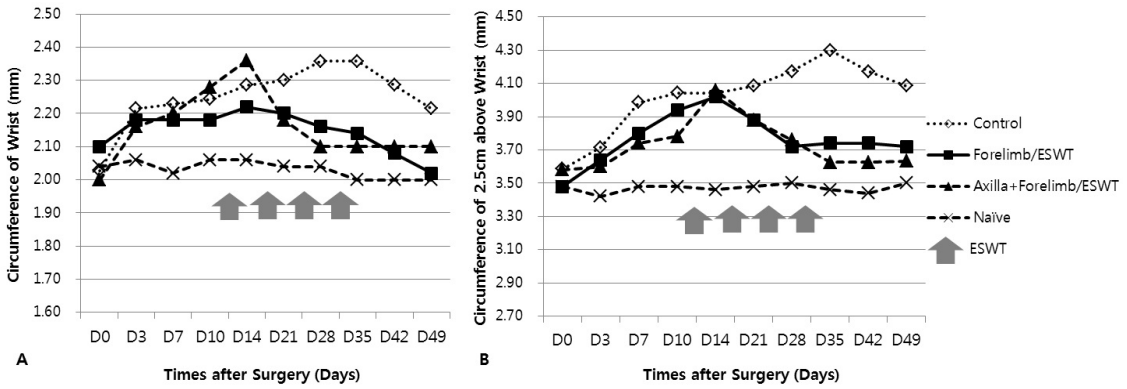

Figure 1. The circumferences of wrist (A) and 2.5 cm above wrist (B) were measured in each group.

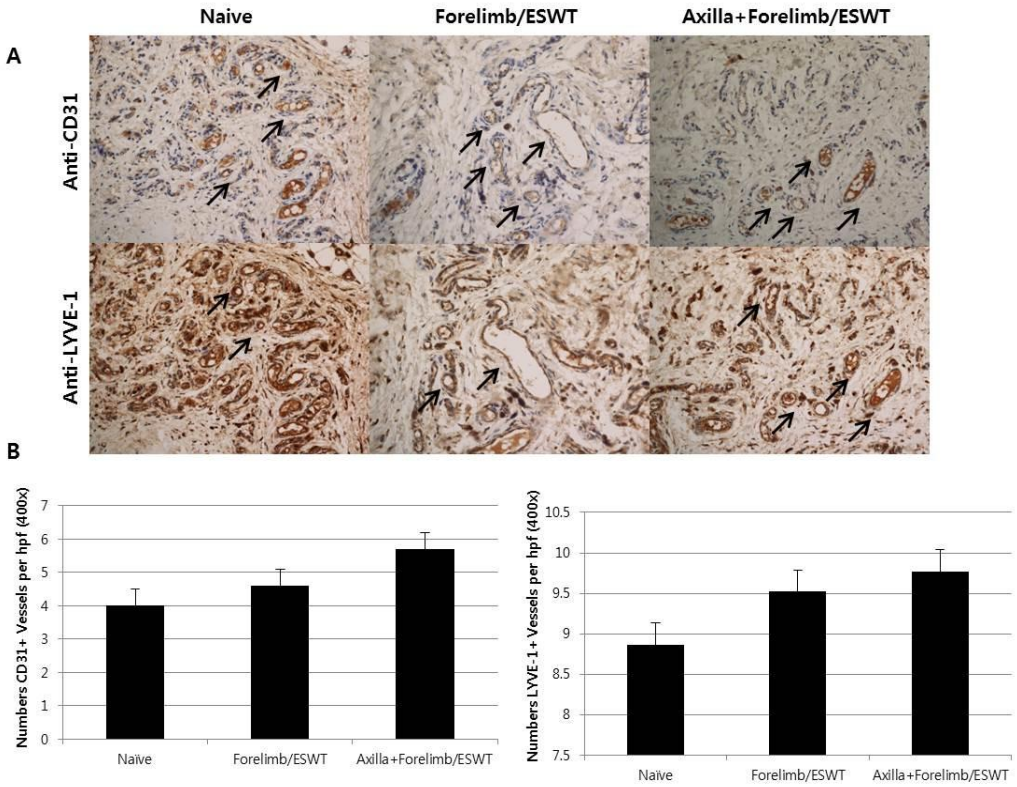

Figure 2. Immunohistochemical analysis of CD31 and LYVE-1 markers in the rat forelimb on 14 days after the last ESWT application. (A) Microscopic immunohistochemistry using anti-CD 31 and LYVE-1 antibodies in ESWT only in lymphedematous forelimb group (Forelimb/ESWT), ESWT in axilla area as well as lymphedematous forelimb group (Axilla+Forelimb/ESWT), and opposite forelimbs that were not induced edema (naïve). The vessels are seen as brown (arrows). (B) Quantification of CD31-positive vessels and LYVE-1-positive vessels in each group. Vessel density measurements were counted the number of CD31-positive and LYVE-1-positive vessels in consecutive 10 high-power fields (hpf) (x400 magnification).

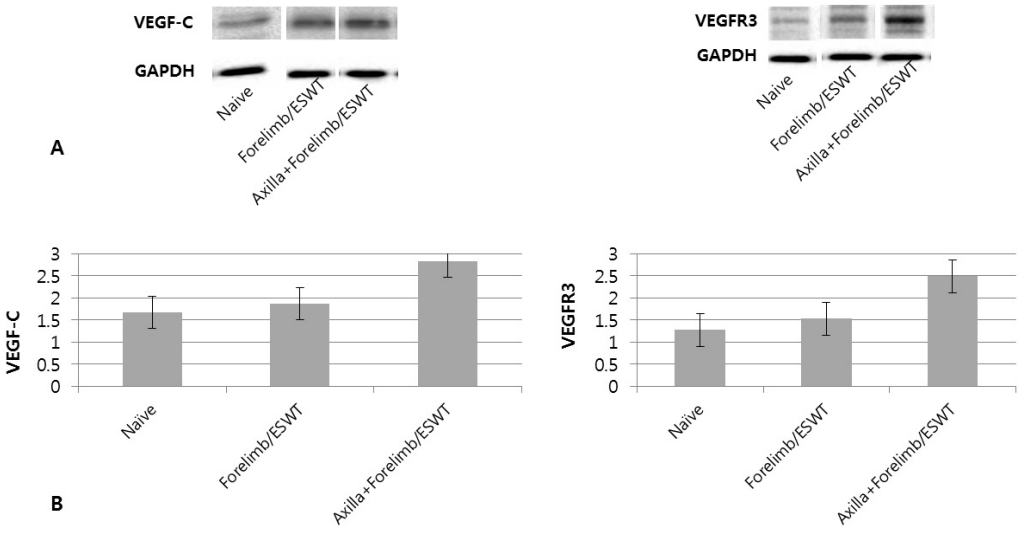

Figure 3. Western blot analysis of VEGF-C and VEGFR3 proteins in the rat forelimb on 14 days after the last ESWT application. (A) Western blot showing VEGF-C and VEGFR3 in lymphedematous forelimb group (Forelimb/ESWT), ESWT in axilla area as well as lymphedematous forelimb group (Axilla+Forelimb), and opposite forelimbs that were not induced edema (naïve). (B) Relative expression of each protein across the different groups.