Original Article

Effectiveness and safety of fractional micro-plasma radio-frequency treatment combined with ablative fractional carbon dioxide laser treatment for hypertrophic scar: a retrospective study

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Background: Hypertrophic scars can be caused by various injuries and lead to a decrease in quality of life of those affected. This study was performed retrospectively in our center to investigate the safety and effectiveness of fractional micro-plasma radio-frequency treatment combined with ablative fractional carbon dioxide (CO_2) laser treatment in patients with hypertrophic scar.

Methods: This was a retrospective study performed in a single center between January 2019 and December 2020. All patients with hypertrophic scars receiving fractional micro-plasma radio-frequency treatment, ablative fractional CO_2 laser treatment, or combined therapy of both were recruited to the study. The participants were then divided into a single therapy group or combined therapy group. The Vancouver scar scale was used to score and subsequently assess the effectiveness of scar treatment and the changes of scar thickness. Some adverse complications were also recorded to evaluate the safety of treatments. A subgroup analysis was then performed to investigate the differences of effectiveness and safety of combined therapy in scar patients at the early stage and late stage.

Results: A total of 64 patients with hypertrophic scars were enrolled in this study, including 45 receiving combined treatment, and 19 receiving single treatment. There was no significant difference in demographic data between the two groups. Notably, combined therapy could more effectively reduce the score of Vancouver scar scale (P=0.026) without significantly increasing the incidence of adverse complications. However, no significant difference was observed in scar thickness between the two groups. Moreover, multiple treatments could further increase the effectiveness of combined therapy according to either the score of Vancouver scar scale or the thickness of scars. Subgroup analysis revealed that combined therapy could reduce the score of Vancouver scar scale and scar thickness in patients much more at the early stage than at the late stage (P=0.032 and 0.042, respectively).

Conclusions: This study revealed that fractional micro-plasma radio-frequency treatment combined with ablative fractional CO_2 laser treatment could be more effective in improving hypertrophic scars then single therapy. Also, multiple treatments could enhance the effectiveness of combined treatment, and patients should be encouraged to receive treatment as early as possible.

Keywords: Fractional micro-plasma radio-frequency treatment; ablative fractional carbon dioxide laser treatment (ablative fractional CO_2 laser treatment); hypertrophic scar; safety; effectiveness; retrospective study

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Introduction

Wound healing is a normal physiological process, however, some wounds caused by surgery, burns, and trauma are prone to heal abnormally, resulting in hypertrophic scars. Hypertrophic scars are mainly caused by the rapid proliferation of fibroblasts and the deposition of excess extracellular collagen (1). Compared with keloid, a hypertrophic scar will be limited to the initial wound site and will not exceed the original boundary (2). According to a previous study, approximately 60% of patients developed hypertrophic scars after surgical procedures (3) and some hypertrophic scars will fade over time. Hypertrophic scars caused by burns are also very common, and the injury to patients is greater due to the randomness and unpredictability of scar site. It has been reported that hypertrophic scar affects 32–72% of burn survivors based on patient age, wound infection, gender, and burn depth (4,5). The formation of hypertrophic scar can lead to unsightly appearance, restricted movement, psychological burden, and abnormal bodily sensations.

At present, the treatment of hypertrophic scar includes both surgical and non-surgical options. Non-surgical treatment is the preferred treatment, and surgical treatment is usually only suitable for the treatment of severe hypertrophic scar. Non-surgical treatments include compression therapy, silicone gels, topical 5-fluorouracil, and steroid injections (6-9). However, due to the half-life of 5-fluorouracil and steroids, they cannot maintain a long-term effect and usually require multiple applications. In addition, due to their side effects, 5-fluorouracil and steroids can only be used limitedly and locally. Silicone gel and compression therapy are more suitable for the prevention of hypertrophic scar.

Fractional micro-plasma radiofrequency technology has been developed for the treatment of hypertrophic scars in recent years. It can trigger rapid re-epithelialization in the epidermis and accelerate the remodeling of fibroblasts. It has been reported to be effective and safe for the treatment for acne scars and hypertrophic scars (10,11). Besides, ablative fractional carbon dioxide (CO_2) laser treatment has also been developed for the treatment of hypertrophic scars by vaporizing water molecules and ablating scars (4). A previous study indicated that ablative fractional CO_2 laser treatment was effective in reducing the thickness of scars and improving the extensibility of involved tissues (12). Recently, more and more attention has been paid to the treatment of hypertrophic scar with a combination of diverse treatments, and therapeutic effects of combined therapy have been investigated.

This study was performed retrospectively in our center to investigate the safety and effectiveness of fractional micro-plasma radio-frequency treatment combined with ablative fractional CO_2 laser treatment in patients with hypertrophic scars. The hypothesis was proposed that the combination of the two methods could effectively remove hypertrophic scars, and would not significantly increase the incidence of adverse complications. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2153).

Methods

Patient selection

This study was a retrospective study performed in a single center of the Affiliated Hospital of Jiangnan University between January 2019 and December 2020. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Hospital of Jiangnan University (No.: 2021081). Individual consent for this retrospective analysis was waived.

Patients with hypertrophic scars due to diverse etiologies were all enrolled in this study. The inclusion criteria encompassed patients who were older than 18 years, younger than 70 years, suffering from serious underlying disease, receiving fractional micro-plasma radio-frequency treatment or ablative fractional CO_2 laser treatment, or combined therapy of both. The following patients were excluded from this study: those younger than 18 years old, older than 70 years old, not receiving either fractional micro-plasma radio-frequency treatment or ablative fractional CO_2 laser treatment, and with incomplete data.

According to the treatments they received, participants were divided into a single treatment and a combined treatments group. Some participants data were collected, including age, gender, etiology of scars, location of scars, time of scar formation, number of treatments, and time between treatments.

Fractional micro-plasma radio-frequency treatment

Fractional micro-plasma radio-frequency treatment was performed using a plasma beam scar therapy apparatus with a roller head (Alma Lasers, Caesarea, Israel) at a power of 60–70 W and a current of 4–6 mA.

Ablative fractional CO_2 laser treatment

Ablative fractional CO_2 laser treatment was performed using an ablative fractional CO_2 laser (Lumenis, Yokneam, Israel). The settings were as follows: density of 5–10%, energy of 15–30 MJ, and a frequency of 300 Hz. The size of light spot and the dose of laser varied based on the size and thickness of scars. The interval between the two treatments was typically about 2–3 months.

Assessments of effectiveness and safety

Participants received outpatient follow-up and the mean duration of follow up was 7.2±2.2 months. The effectiveness of scar treatment was assessed by the score of the Vancouver scar scale and the changes of scar thickness. The Vancouver scar scale contains four items, including pigmentation (0–3 points), vascularity (0–3 points), pliability (0–5 points), and height (0–4 points), with a total score of 15 points. The thickness of scars was measured using a high-frequency ultrasound device. Some adverse complications were also recorded to evaluate the safety of treatments, such as pruritus, pain, seepage, bleeding, and swelling.

Subgroup analysis

A subgroup analysis was performed to investigate the differences in effectiveness and safety of combined therapy in scar patients at different stages. Participants who received treatment within 6 months postinjury were defined as early stage while those receiving treatment more than 6 months postinjury were defined as late stage. Then, the differences of effectiveness and safety of combined therapy in these subgroups were analyzed.

Statistical analysis

The statistical analysis in this study was performed using SPSS 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were reported as mean with standard deviation (SD) and analyzed using two-tailed Mann-Whitney U test for comparisons between two groups or subgroups. Categorical variables were reported as numbers and percentages and analyzed using chi-square (χ^2) tests. A P value less than 0.05 was considered statistically significant.

Results

There were 196 patients admitted to our center for the treatment of hypertrophic scars between January 2019 and December 2020 (*Figure 1*). Among them, 132 patients were eliminated based on the exclusion criteria. Finally, 64 patients with hypertrophic scars were enrolled in this study, including 45 who received fractional micro-plasma radio-frequency treatment combined with ablative fractional CO_2 laser treatment, and 19 who received either treatment singly.

Participant demographic data are listed in *Table 1*. The mean age in the single therapy group was 35.2±11.3 years, and that in combined therapy group was 34.6±13.6 years. More than two-thirds of participants in both groups were male and the most common etiology of hypertrophic scars in this study was burn. The most common location of scars in both groups was head and/or neck, followed by extremity and trunk. The time of scar formation was 8.1± 2.0 months in the single therapy group and 7.4±2.6 months in the combined therapy group. A total of 10 participants received only 1 treatment in the single therapy group, 4 participants received 2 treatments, and 5 received more than 2 treatments. In the combined therapy group, 19 participants received 1 treatment, 16 received 2 treatments, and 10 received more than 2 treatments. The interval between treatments was 2.4±0.7 months in the single therapy group and 2.1±0.9 months in the combined therapy group. Generally, there was no significant difference in demographic data between the two groups.

The effectiveness of single therapy and combined therapy were assessed using the score of Vancouver scar scale and the changes of scar thickness, as summarized in *Table 2*. Both single therapy and combined therapy could significantly improve hypertrophic scars in participants according to the score of Vancouver scar scale (P=0.044 and P<0.001). Notably, combined therapy could more

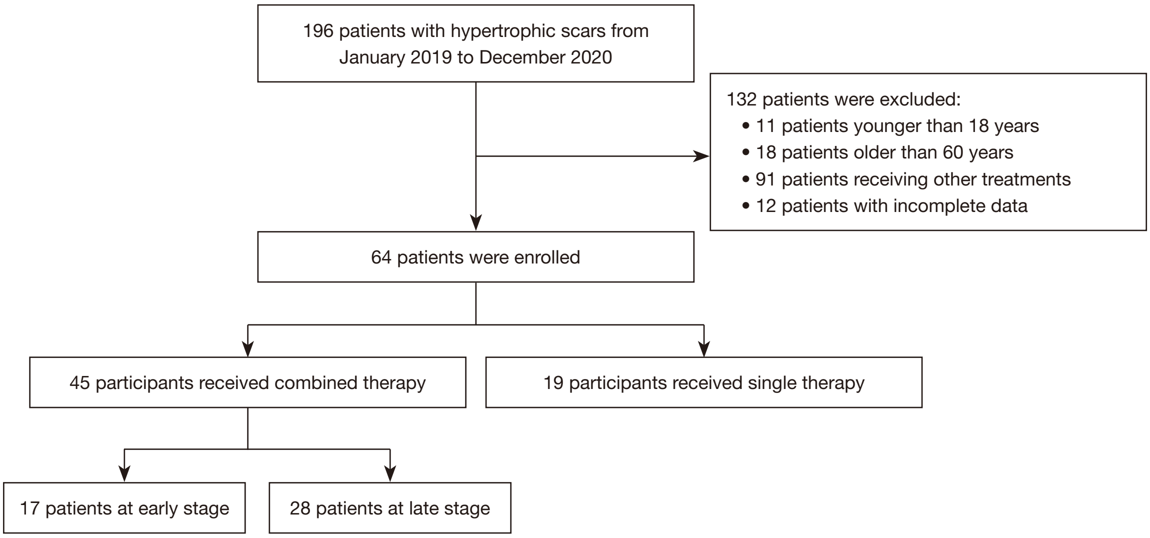

Figure 1 Flow chart of study.

Table 1 Overview of participant demographic data according to therapy

Demographics	Single therapy	Combined therapy	P value
Number	19	45	
Age, year	35.2±11.3	34.6±13.6	0.090
Gender, n (%)			0.690
Male	13 (68.4)	33 (73.3)	
Female	6 (31.6)	12 (26.7)	
Etiology of scars, n (%)			0.828
Burn	11 (57.9)	31 (68.9)	
Surgical procedures	3 (15.8)	6 (13.3)	
Chemical agent	2 (10.5)	5 (11.1)	
Electricity	2 (10.5)	2 (4.4)	
Other	1 (5.3)	1 (2.2)	
Location of scars, n (%)			0.955
Head and/or neck	9 (47.4)	20 (44.4)	
Trunk	4 (21.1)	11 (24.4)	
Extremity	6 (31.6)	14 (31.1)	
Time of scar formation, month	8.1±2.0	7.4±2.6	0.525
Number of treatments, n (%)			0.518
1	10 (52.6)	19 (42.2)	
2	4 (21.1)	16 (35.6)	
>2	5 (26.3)	10 (22.2)	
Interval between treatments, month	2.4±0.7	2.1±0.9	0.159

Table 2 Effectiveness of single or combined therapy for hypertrophic scars

Demographics	Single therapy	Combined therapy	P value[b]
Total score of Vancouver scar scale			
Before	8.5±2.0	8.9±1.5	0.617
After	7.5±1.8	7.5±1.5	0.845
P value[a]	0.044	<0.001	
Change	0.9±0.5	1.4±0.7	0.026
Pigmentation			
Before	1.9±0.7	2.0±0.6	0.464
After	1.6±0.5	1.6±0.6	0.932
P value[a]	0.047	0.018	
Change	0.3±0.5	0.4±0.5	0.416
Vascularity			
Before	1.7±0.7	1.7±0.7	0.786
After	1.5±0.5	1.6±0.5	0.833
P value[a]	0.200	0.520	
Change	0.2±0.4	0.2±0.4	0.850
Pliability			
Before	2.1±0.6	2.2±0.6	0.471
After	1.8±0.6	1.8±0.7	0.909
P value[a]	0.051	0.033	
Change	0.3±0.5	0.4±0.5	0.305
Height			
Before	2.8±0.7	2.9±0.9	0.659
After	2.5±0.6	2.5±0.7	0.937
P value[a]	0.087	0.048	
Change	0.3±0.6	0.4±0.5	0.558
Scar thickness, mm			
Before	6.7±1.9	6.8±2.4	0.923
After	3.1±1.0	3.0±0.8	0.553
P value[a]	<0.001	<0.001	
Change	3.6±0.9	3.8±1.0	0.455

[a], comparison between the score of Vancouver scar scale before and after the treatment; [b], comparison between the score of Vancouver scar scale in different groups.

effectively improve hypertrophic scars and reduce the score of Vancouver scar scale compared with single therapy (P=0.026), although no other significant difference was found in the comparisons of four detailed items. In addition, both therapies could dramatically reduce the thickness of scars (both P<0.001); however, no significant difference was observed between the two groups.

The impacts of number of treatments on the

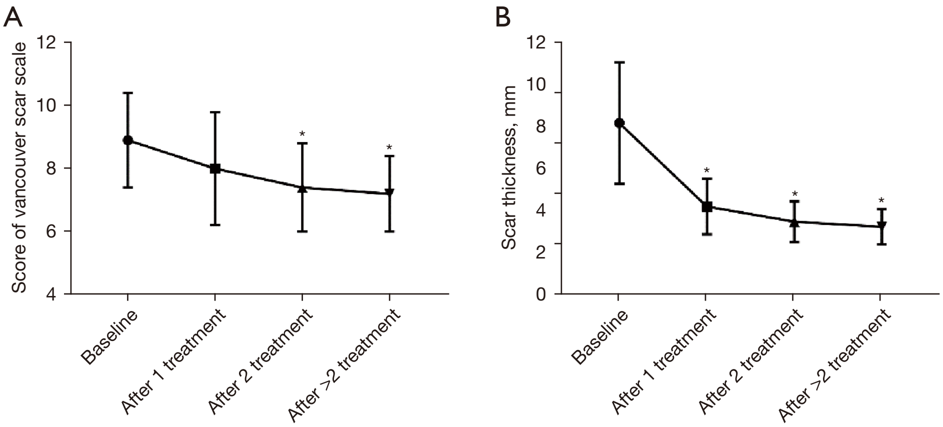

Figure 2 Effectiveness of multiple treatments for hypertrophic scars. (A) Changes of Vancouver scar scale scores after multiple treatments; (B) changes of scar thickness after multiple treatments. *, P<0.05.

Table 3 Adverse complications in participants

Demographics	Single therapy, n (%)	Combined therapy, n (%)	P value
Pruritus	4 (21.1)	12 (26.7)	0.599
Pain	1 (5.3)	3 (6.7)	0.659
Seepage	4 (21.1)	7 (15.6)	0.420
Bleeding	3 (15.8)	7 (15.6)	0.624
Swelling	1 (5.3)	4 (8.9)	0.532
Total	13 (68.4)	32 (71.1)	0.891

effectiveness of combined therapy was then assessed (*Figure 2*). It was found that multiple treatments could further increase the effectiveness of combined therapy in improving hypertrophic scars, according to either the score of Vancouver scar scale or the thickness of scars.

Adverse complication data were collected to assess the safety of combined therapy (*Table 3*). The incidence of total adverse complications was 71.1% (32 cases) and 68.4% (13 cases), in the single therapy and combined therapy groups, respectively, showing no significant difference between them. The most common complication in both groups was pruritus, followed by seepage, and bleeding.

Next, participants in the combined therapy group were divided into two subgroups, an early stage subgroup and a late stage subgroup. Generally, there was no significant difference between the two groups, as shown in *Table 4*, except the time of scar formation. The effectiveness of combined therapy in different subgroups was assessed according to the score of Vancouver scar scale and the changes of scar thickness (*Table 5*). Combined therapy was found to be significantly effective at improving hypertrophic scars in patients at the early stage or late stage. More importantly, combined therapy could reduce the score of Vancouver scar scale by 1.7±0.7 points in patients at the early stage, much more than the 1.3±0.6 points in patients at the late stage (P=0.032). Similarly, combined therapy could reduce scar thickness by 4.2±0.8 mm in patients at the early stage, much more than the 3.7±0.9 mm in patients at the late stage (P=0.042).

Discussion

To our knowledge, this is the first study to date investigate the effectiveness and safety of fractional micro-plasma radio-frequency treatment combined with ablative fractional CO_2 laser treatment in patients with hypertrophic scarring. It was found that combined therapy could more effectively improve hypertrophic scars than single treatment

Table 4 Overview of participant demographic data according to stage

Demographics	Early stage	Late stage	P value
Number	17	28	
Age, year	34.0±10.4	34.8±13.5	0.237
Gender, n (%)			0.496
Male	13 (76.5)	20 (71.4)	
Female	4 (23.5)	8 (28.6)	
Etiology of scars, n (%)			0.375
Burn	13 (76.5)	18 (64.3)	
Surgical procedures	1 (5.9)	5 (17.9)	
Chemical agent	2 (11.8)	3 (10.7)	
Electricity	0 (0.0)	2 (7.1)	
Other	1 (5.9)	0 (0.0)	
Location of scars, n (%)			0.318
Head and/or neck	10 (58.9)	10 (35.7)	
Trunk	3 (17.6)	8 (28.6)	
Extremity	4 (23.5)	10 (35.7)	
Time of scar formation, month	4.6±1.5	9.0±1.6	<0.001
Number of treatments, n (%)			0.524
1	9 (52.9)	10 (35.7)	
2	5 (29.4)	11 (39.3)	
>2	3 (17.6)	7 (25.0)	
Interval between treatments, month	2.2±0.8	2.1±1.1	0.105

Table 5 Effectiveness of combined therapy on patients with hypertrophic scars at different stages

Demographics	Early stage	Late stage	P value[b]
Total score of Vancouver scar scale			
Before	8.8±1.3	9.1±1.6	0.517
After	7.1±1.3	7.8±1.5	0.118
P value[a]	<0.001	0.003	
Change	1.7±0.7	1.3±0.6	0.032
Scar thickness, mm			
Before	7.0±2.3	6.8±2.4	0.891
After	2.8±0.8	3.1±0.9	0.140
P value[a]	<0.001	<0.001	
Change	4.2±0.8	3.7±0.9	0.042

[a], comparison between the score of Vancouver scar scale before and after the treatment; [b], comparison between the score of Vancouver scar scale in different groups.

therapy. The incidence of adverse complications was similar between the combined and single therapy groups. A further subgroup analysis was also performed which revealed that patients at the early stage could experience more significant improvement after the treatment of combined therapy.

Ablative fractional CO_2 laser technology has been employed for many years; however, it is only in recent years that this technique has been applied to the treatment of hypertrophic scars (3,4,13-19). Several case reports firstly reported the effectiveness of ablative fractional CO_2 laser treatment for hypertrophic scars (20,21), then Makboul *et al.* enrolled 40 patients with hypertrophic scars and confirmed ablative fractional CO_2 laser treatment as a feasible management for hypertrophic scarring (22). Over the recent years, combined therapies of some other treatments and ablative fractional CO_2 laser treatment have also been developed to increase the effectiveness in improving hypertrophic scars. Huang *et al.* combined ablative fractional CO_2 laser treatment with 5-fluorouracil ethosomal gel treatment in a rabbit model; however, it was found that combined therapy was not superior to single therapy of ablative fractional CO_2 laser treatment (17). Zhang *et al.* found in their rabbit model that artesunate combined with ablative fractional CO_2 laser effectively reduces hypertrophic scarring (14). Ablative fractional CO_2 laser combined with a variety of laser therapy, such as 595-nm pulsed dye laser, can also better increase the effectiveness of the treatment of hypertrophic scars (15).

Fractional micro-plasma radio-frequency technology was developed before 2008 and initially used for the treatment of facial scars and rhytids in 2010 (23,24). It was subsequently used for the treatment of post-burn facial hyperpigmentation, abdominal striae, and atrophic acne scar, and provided a promising noninvasive treatment (11,25,26). Fractional micro-plasma radio-frequency treatment also was also shown to enhance the improvement of hypertrophic scars (27). A rabbit model indicated that fractional micro-plasma radio-frequency treatment could improve the color and texture and reduce microvessels in the scar tissue by reducing the level of interleukin-8 and macrophage chemoattractant protein-1 (11). It has previously been shown that fractional micro-plasma radio-frequency treatment combined with triamcinolone could improve the effectiveness of hypertrophic scar reduction (27).

Previously, there have been no reports about the combination of fractional micro-plasma radio-frequency and ablative fractional CO_2 laser in the treatment of skin diseases. In this study, we found that multiple treatments significantly increased the effectiveness of combined treatment, which was similar to the findings of a previous study. Kemp Bohan *et al.* reported that two treatments were required to achieve a significant reduction of scar thickness when using ablative fractional CO_2 laser for the treatment of hypertrophic burn scar (4). This may explain why no significant difference was observed in scar thickness between the two groups. Also, we found that patients with early stage hypertrophic scars could achieve better effectiveness after the treatment of combined therapy. Tan *et al.* also reported in their study that patients receiving treatments within 1 month postinjury were the most optimal patients for laser treatments (13). It was also found that patients receiving treatments more than 12 months postinjury may benefit from laser treatment (13). However, most patients in our study received treatments within 12 months after injury and this conclusion cannot be verified. The most important precaution of combined treatment in this study was to closely monitor the occurrence of any complication or adverse event in patients and take remedial measurements in time.

The limitations in this study should be noted. Firstly, this study was performed in a single center, so the sample size in this study was not large enough to further analyze the effectiveness of combined therapy using regression analysis. Some potential factors may have affected the final results in this study. A multicenter study would compensate for this limitation. Secondly, hypertrophic scars were caused by different etiologies in this study. Different etiologies may also affect the effectiveness of combined or single therapies. However, the inclusion of hyperplastic scars with only 1 etiology would have led to a serious shortage of sample size. A larger sample size would better enable the investigation of the effectiveness of combined therapy in improving hypertrophic scar caused by a certain etiology. Thirdly, most participants received treatment within 12 months postinjury. Therefore, early stage was defined as within 6 months postinjury. Different definitions may also affect the effectiveness of combined therapy but so far it has not been unified.

In conclusion, this study confirmed that combined therapy was more effective in improving hypertrophic scars than single therapy without significantly increasing the incidence of adverse complications. Furthermore, multiple treatments can be recommended for patients with severe hypertrophic scars to further improve the effectiveness and patients should be encouraged to receive treatment at an early stage.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-2153

Data Sharing Statement: Available at https://dx.doi.org/10.21037/apm-21-2153

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-2153). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Hospital of Jiangnan University (No.: 2021081). Individual consent for this retrospective analysis was waived.

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