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ORIGINAL ARTICLE

Change in PsAID-12 scores in patients continuing or discontinuing anti-TNF treatments in psoriatic arthritis: results from the HUR-BIO biologic registry

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Abstract

Objective Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID-12) has been developed to be used in psoriatic arthritis in daily practice. The aim of the present study was to assess the change values of PsAID-12 in PsA patients continuing or discontinuing anti-TNF treatment.

Methods We recruited patients from the Hacettepe University biological database (HUR-BIO). Overall, 70 PsA patients had PsAID-12 score before the initiation of the first anti-TNF treatment. Stopping or switching the anti-TNF treatment due to inefficacy was definitely considered a negative response. Changes were evaluated by the comparison with the baseline PsAID-12 score in compliance with the favorable and unfavorable responses to anti-TNF treatments. The standardized response mean (SRM) was used for determining the response.

Results Seventy (78.6% female) patients were analyzed and their mean age was 45.5 years (12.0 years). The mean follow-up duration was 18.3 months (12.6 months). At baseline, the mean PsAID-12 score was 6.6 (1.5). Physicians stopped or switched the treatment in 28 patients (40.0%) due to the inefficacy of anti-TNF treatment. The ΔPsAID-12 score was 0.25 (1.71) in the patients discontinuing anti-TNF treatment and 3.52 (2.31) in the patients continuing their anti-TNF treatment ($p < 0.001$). The SRM scores higher for PsAID-12, particularly in the well response to anti-TNF treatments.

Conclusion A decrease of 3.5 units in PsAID-12 score shows a favorable response to anti-TNF treatment. Changes in PsAID-12 score had well discrimination capacity for anti-TNF treatments.

Keywords Anti-TNF treatment · Biological registry · PsAID-12 · Psoriatic arthritis

Introduction

Psoriatic arthritis (PsA) is a chronic rheumatologic disease that affects the skin, joints, entheseal regions, spine, and nails [1]. Conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs) and/or biologic DMARDs can be used to treat PsA patients [1]. Anti–tumor necrosis factor alpha (TNF-α) drugs are still the first-line biologic DMARD therapy for PsA patients who do not respond to conventional DMARD therapies [2, 3]. The target of PsA treatments is achieving low disease activity or remission [2, 3]. Various composite indices and patient-reported outcomes can be used to define treatment targets [4].

The international rheumatology specialists and patients' partners developed a new patient-reported outcome score in 2014 to test the disease impact of PsA [5]. Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID-12) is a patient-reported outcome measure, in which each question has its own specific value, and has two main compartments, which are physical and psychosocial domains. PsAID-12 has been developed for daily clinical practice. In the original study, it was indicated that PsAID-12 could be used for the determination of PsA treatment [5]. There is still a need to determine PsAID-12 cutoff values to interpret treatment changes. Although the original study determined a cut-off value, no information has been reported on its use for

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determining a response to biologic DMARD therapy, yet, in daily clinical practice. Accordingly, the purpose of this study was to assess the change values of PsAID-12 in PsA patients continuing or discontinuing anti-TNF treatment in a biological registry.

Materials and methods

Selection of patients

The present study included patients who were registered in the Hacettepe University biological database (HUR-BIO), which was established in 2005 [6]. In this database, there were 319 patients who were under an anti-TNF drug for PsA, at any time during their treatment periods. Since January 2013, PsAID-12 score has also been calculated in the HUR-BIO database and patients filled up all outpatient visits including pre-treatment visits. The Turkish version of PsAID-12 score was applied for 116 PsA patients before starting the first anti-TNF treatment and we enrolled 88 of them, whose PsAID-12 score was 4 and above, in the study. However, 18 patients were excluded as 12 of them did not have follow-up visits, 3 of them had started their treatments in the last 3 months, and 3 of them had follow-up visits but did not have PsAID-12 scores. Therefore, we included 70 PsA patients in the analysis.

Assessments on baseline and follow-up visits

Demographic features of PsA patients were noted before anti-TNF treatment. For this purpose, age, sex, duration of education, duration of psoriasis, duration of PsA, family history of psoriasis and PsA, body mass index (BMI), and smoking status were recorded. Data of current treatment regimen including anti-TNF drugs (adalimumab, certolizumab, etanercept, golimumab, and infliximab), all synthetic DMARDs (methotrexate, sulfasalazine, leflunomide, and hydroxychloroquine), and glucocorticoids were recorded as well. The number of swollen and tender joints (28 joints), acute-phase response (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)), Disease Activity Score-28 (DAS-28) [4], Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [7], Bath Ankylosing Spondylitis Functional Index (BASFI) [8], Health Assessment Questionnaire Disability Index (HAQ-DI) [4], pain-Visual Analogue Scale (VAS), Patient Global Assessment Of Disease Activity (PGA)-VAS, fatigue-VAS, morning stiffness-VAS, and PsAID-12 score were used for the assessment of PsA disease activity. Dermatological assessment was done by using skin activity VAS score and Dermatological Life Quality Index (DLQI) [4]. PsA disease activity was assessed before starting anti-TNF treatment, during stopping or switching to anti-TNF treatments, and in the last control visit for patients continuing anti-TNF treatments.

Decision of anti-TNF treatment and utilization of PsAID-12

Initiation and continuation of anti-TNF treatments Patients who were prescribed an anti-TNF drug were followed up in their routine clinical visits. The decision of continuing, stopping, or switching to another anti-TNF drug was made by clinicians with patients' agreements. There were six rheumatology specialists who could determine these kinds of decisions in the HUR-BIO registry. The clinicians were not blinded to the assessment of PGA, pain-VAS, fatigue-VAS, DAS-28, BASDAI, HAQ-DI, and PsAID-12; however, they used their own judgment to decide whether to continue or stop the treatment. In each control visit, it was noted whether the reason for switching to another anti-TNF drug was due to inefficacy or not.

Favorable response to anti-TNF treatment According to the baseline evaluation, a decrease of 20 mm and above in pain-VAS score and PGA, an improvement of 0.22 units and above in HAQ-DI score, a decrease of 20 mm and above in BASDAI score, a decrease of 50% in BASDAI score, or a decrease of 1.2 units and above in DAS-28 score was considered as a favorable response to anti-TNF treatment.

To demonstrate the activity for determining the response to the treatment, standardized response mean (SRM) was used.

The study was approved by the Ethics Committee of Hacettepe University Faculty of Medicine (No. GO 15/788) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from all patients included in the study.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (IBM Corp., Armonk, NY, USA) version 22 for Windows. The acceptability of the data against normal distribution was checked by the Shapiro-Wilk analysis test. Distribution of measurable (quantitative) data was expressed as mean (standard deviation). Variables that did not fit normal distribution were expressed by median and minimum–maximum values. Student's t test was used to evaluate the difference between patient and control groups for the normal distribution–matched data.

Chi-square test was used for the evaluation of categorical variables in the findings of patient and control groups. The distribution of countable data was expressed as % (percent). SRM was computed by dividing the mean score change (i.e., follow-up minus baseline) by the standard deviation of the change. The relationship of PsAID-12 with BASDAI, PGA, BASFI, pain-VAS, HAQ-DI, DLQI, fatigue-VAS, morning stiffness, ESR, and CRP was evaluated using Spearman's

Table 1 Demographic features and baseline assessments before the start of anti-TNF treatment

	All group $n = 70$ (mean ± SD)	Anti-TNF continued $n = 42$ (mean ± SD)	Anti-TNF stopped/switched $n = 28$ (mean ± SD)	p
Age (years)	45.5 (12.0)	46.0 (12.0)	44.6 (12.3)	0.63
Female gender (%)	78.5	71.4	89.2	0.74
PsA diagnosis duration	5.3 (4.4)	5.5 (2.9)	5.1 (5.3)	0.85
DAS-28	4.07 (1.22)	4.14 (1.23)	3.96 (1.21)	0.55
HAQ-DI	0.86 (0.53)	0.81 (0.53)	0.94 (0.53)	0.33
BASDAI	6.5 (1.7)	6.5 (1.9)	6.5 (1.5)	0.87
BASFI	4.9 (2.4)	4.7 (2.4)	5.3 (2.4)	0.29
ESR	22 (17)	25 (19)	17 (11)	0.76
CRP	2.3 (2.8)	2.8 (3.3)	1.5 (1.9)	0.052
Morning stiffness-VAS	5.1 (3.5)	4.8 (3.6)	5.4 (3.4)	0.51
DLQI	9.3 (8.7)	11.0 (9.7)	6.3 (5.9)	0.047
Pain-VAS	6.9 (2.1)	7.0 (2.1)	6.7 (2.0)	0.44
PGA-VAS	6.4 (1.7)	6.5 (1.8)	6.4 (1.6)	0.79
Fatigue-VAS	6.5 (2.5)	6.6 (2.3)	6.4 (2.9)	0.75
Skin-VAS	4.8 (3.3)	5.3 (3.5)	3.5(3.1)	0.19
PsAID-12	6.6 (1.5)	6.6 (1.7)	6.7 (1.3)	0.67

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; *BASFI*, Bath Ankylosing Spondylitis Functional Index; *CRP*, C-reactive protein (mg/dl); *DAS-28*, Disease Activity Score-28; *DLQI*, Dermatological Life Quality Index; *ESR*, erythrocyte sedimentation rate (mm/h); *HAQ-DI*, Health Assessment Questionnaire Disability Index; *PsAID*, Psoriatic Arthritis Impact of Disease; *VAS*, Visual Analogue Scale

correlation test. In all tests, p values below 0.05 were considered statistically significant.

Results

General features

Seventy patients (78.6% female) with a mean age of 45.5 years (12.0 years) were followed up for a mean of 18.3 months (12.6 months). A total of 213 clinical visits were performed with a median 3 (1–8) control visits. In the follow-up period, 28 (40.0%) patients stopped their first anti-TNF treatments or switched to another anti-TNF treatment. The demographic features and baseline assessments before the initiation of the anti-TNF treatments are presented in Table 1. Of the patients, 48 (68.6%) had an education duration of 8 years and above and 34 (48.6%) patients were obese; 36 out of 54 (66.7%) patients smoked. The mean BMI was 29.7 (5.9). Using conventional synthetic DMARDS before the anti-TNF treatments were determined, 60 (85.7%) patients used methotrexate, 44 (62.9%) patients used sulfasalazine, 29 (41.4%) patients used hydroxychloroquine, 25 (35.7%) patients used leflunomide, and 50 (71.4%) patients used glucocorticoids. The first anti-TNF agent was adalimumab in 33 (47.1%) patients, etanercept in 13 (18.6%) patients, golimumab in 11 (15.7%) patients, infliximab in 7 (10.0%) patients, and certolizumab in 6 (8.6%) patients.

Favorable response to anti-TNF treatment and PsAID-12 results

Patients who reached the level of favorable response rate according to pain-VAS, PGA, BASDAI, DAS-28, and HAQ-DI scores are presented in Table 2. Physicians stopped or switched the treatment in 28 patients (40.0%) due to the inefficacy of anti-TNF treatment. The decrease in PsAID-12 score

Table 2 Favorable response to anti-TNF treatment and PsAID-12 results

Level of favorable response to anti-TNF treatments	Patients with anti-TNF continuing	ΔPsAID-12
ΔPain ≥ 20 mm	Yes $n = 40$	3.1 (2.4)
	No $n = 30$	0.8 (2.1)
ΔPGA ≥ 20 mm	Yes $n = 40$	2.9 (2.5)
	No $n = 30$	0.9 (2.2)
ΔBASDAI ≥ 20 mm	Yes $n = 34$	3.5 (2.6)
	No $n = 36$	0.7 (1.6)
ΔHAQ-DI ≥ 0.22	Yes $n = 31$	3.5 (2.3)
	No $n = 39$	1.0 (2.0)
ΔDAS-28 ≥ 1.2	Yes $n = 31$	3.4 (2.6)
	No $n = 33$	0.9 (1.9)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; *DAS-28*, Disease Activity Score-28; *HAQ-DI*, Health Assessment Questionnaire Disability Index; *PsAID*, Psoriatic Arthritis Impact of Disease; *VAS*, Visual Analogue Scale

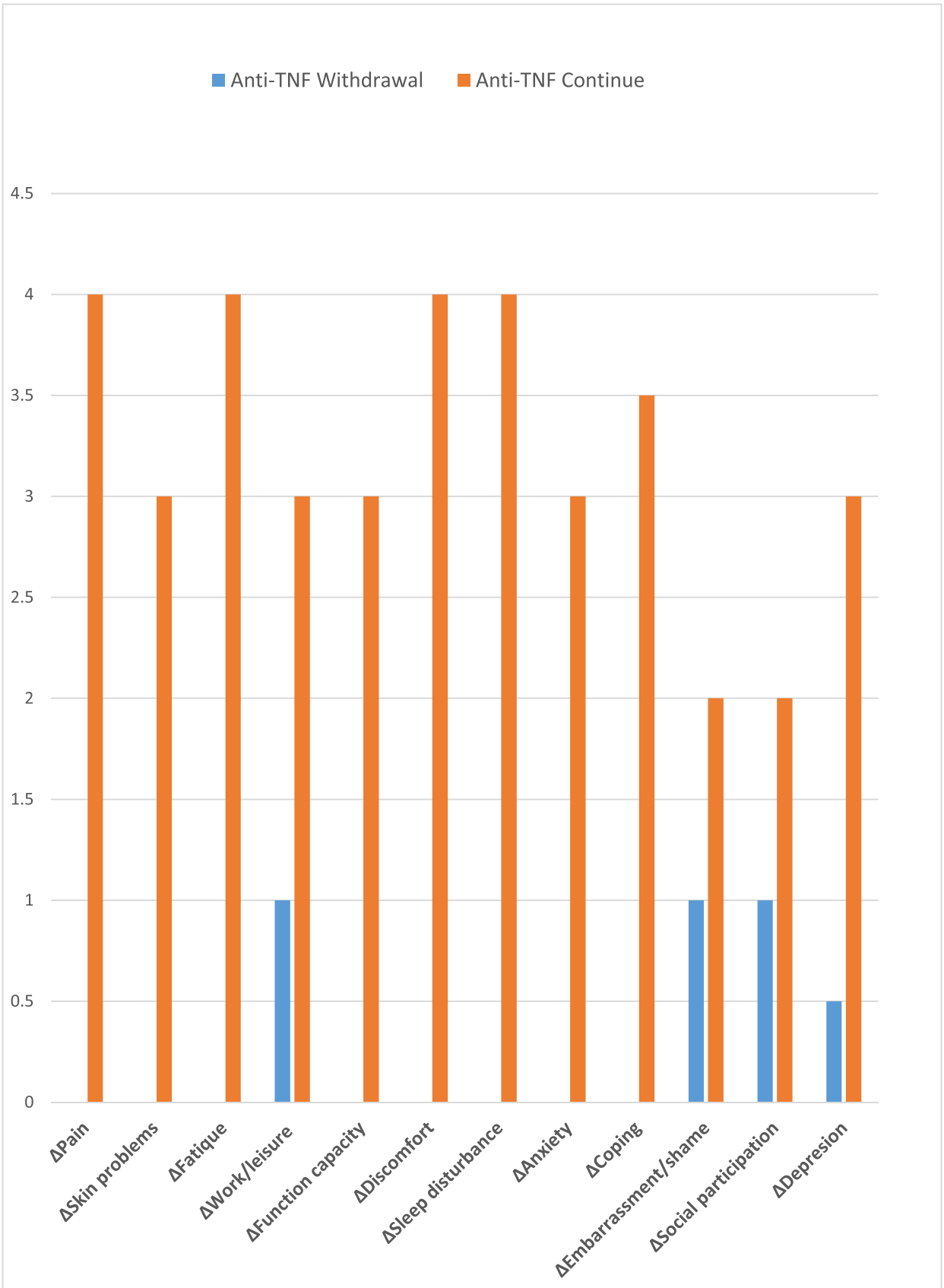

Fig. 1 Change in PsAID-12 score for each item

was 0.25 (1.71) units in the patients discontinuing anti-TNF treatment, while the decrease was 3.52 (2.31) units in the patients continuing their anti-TNF treatment ($p < 0.001$). The change in PsAID-12 score for each item is given in Fig. 1. For all outcome measures, SRMs according to the anti-TNF treatments are given in Table 3.

Correlation between changes in the indication parameters

In the follow-up visits, the correlations between ΔPsAID-12 score with other outcome measures were as follows: ΔHAQ-DI ($r = 0.63$), Δpain-VAS ($r = 0.63$), ΔBASDAI ($r = 0.61$), ΔDAS-28 ($r = 0.59$), ΔPGA ($r = 0.59$), ΔDLQI ($r = 0.55$), Δfatigue-VAS ($r = 0.48$), ΔBASFI ($r = 0.46$), Δmorning stiffness ($r = 0.45$), ΔESR ($r = 0.37$), and ΔCRP ($r = 0.24$).

Discussion

The impact of PsA has both physical and psychosocial effects on patients. Significant levels of improvement are achieved in physical complications of PsA patients during anti-TNF treatments. There is also a positive psychosocial impact on loss of workforce, decrease in depression, and improvement of sleep disturbance. Importantly, PsAID-12 is a score that represents the evaluation of both physical and psychosocial conditions and that displays the impact of disease on a patient's life. Recently, the utilization of PsAID-12 in the evaluation of response to DMARD treatments has been investigated in four different studies [9–12]. However, no data is available whether PsAID-12 can be used in daily practice to determine treatment decision in a biological registry. The present study suggests that the PsAID-12 can be effectively used when to decide stopping or switching anti-TNF treatment of a PsA patient.

In the original PsAID study, 3-unit decrement in PsAID-12 was found as a cutoff value for a minimal clinically relevant improvement [5]. Fortunately, more biologic DMARD options are now available and if clinicians continue the first anti-TNF treatment for their patients, patients would have an acceptable or well response to treatments. From this aspect, in the present study, PsAID-12 score decreased by a mean of 3.5 units in the patients continuing their anti-TNF treatment. Almost similar results were found for other parameters indicating a favorable response to treatment, for instance, a decrease of 3.1 units for pain-VAS, 2.9 units for PGA, 3.5 units for HAQ-DI, and 3.4 for DAS-28. Overall, all these findings suggest that PsAID-12 is acceptable patient-reported outcome measure that can be used in daily practice for interpretation of continuing or stopping anti-TNF treatments. SRM shows a discriminant capacity of one outcome measure. Similar to other studies [5, 12], the results of the present study showed that PsAID-12 had better sensitivity to change capacity regarding other outcome measures, such as DAS-28, pain-VAS, and PGA-VAS. Importantly, SRM was excellent among the patients who had favorable response to anti-TNF treatments. SRM for PsAID-12 score was 0.90 in the original study and 0.74 in the study by Holland et al. [12]; those were comparable with the results of the present study.

There were limitations in the present study. In the original study, PsAID-12 score was defined as 4 and above to represent active disease level [5]. However, in daily practice, PsAID-12 score was under 4 in approximately 25% of the

Table 3 Standardized response means according to the anti-TNF treatments

	All patients $n = 70$	Anti-TNF continuing patients $n = 42$	Anti-TNF stopping patients $n = 28$
PsAID-12	0.84	1.51	0.14
DAS-28	0.79	1.26	0.29
BASDAI	0.77	1.41	0.13
Pain	0.75	1.32	0.13
PGA	0.71	1.16	0.12
BASFI	0.63	1.30	−0.12
Fatigue-VAS	0.49	0.97	−0.21
HAQ-DI	0.45	1.02	−0.11
Morning stiffness-VAS	0.45	0.78	−0.01
CRP	0.45	0.56	0.23
DLQI	0.40	0.60	0.05
ESR	0.34	0.60	−0.07

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; *BASFI*, Bath Ankylosing Spondylitis Functional Index; *CRP*, C-reactive protein (mg/dl); *DAS-28*, Disease Activity Score-28; *DLQI*, Dermatological Life Quality Index; *ESR*, erythrocyte sedimentation rate (mm/h); *HAQ-DI*, Health Assessment Questionnaire Disability Index; *PsAID*, Psoriatic Arthritis Impact of Disease; *VAS*, Visual Analogue Scale

patients before starting anti-TNF treatment. In this group of patients, the precision of PsAID-12 was not expressed in the determination of treatment response. In the present study, 28 tender and swollen joints and DAS-28 score were evaluated to assess disease activity. However, 66/68 joints are usually preferred, and this is another limitation of our study.

In conclusion, a decrease of 3.5 units in PsAID-12 score indicates a favorable response to anti-TNF treatment in real-life biological registry. PsAID-12 reveals a strong impact of the disease on a patient's life from both physical and psychosocial aspects. Besides showing a close relationship with other patient-reported outcome measures often used in PsA treatment, PsAID-12 appears to be an effective composite index for maintaining a response to the treatment. There is a need for further randomized controlled trials to test the use of PsAID-12 in daily practice.

Compliance with ethical standards

The study was approved by the Ethics Committee of Hacettepe University Faculty of Medicine (No. GO 15/788) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from all patients included in the study.

Disclosures None.

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