

Impact of Bariatric Surgery on Moderate to Severe Psoriasis: A Retrospective Nationwide Registry Study

Marta LASKOWSKI^{1,2}, Linus SCHIÖLER³, Johan OTTOSSON⁴, Marcus SCHMITT-EGENOLF⁵, Ann-Marie WENNBERG^{1,2}, Torsten OLBERS^{6,7}, Kjell TORÉN³,⁸ and Helena GUSTAFSSON^{2,9}

¹Department of Dermatology and Venereology, Institute of Clinical Sciences, The Sahlgrenska Academy, University of Gothenburg, ²Department of Dermatology and Venereology, Region Västra Götaland, Sahlgrenska University Hospital, ³Occupational and Environmental Medicine, School of Public Health and Community Medicine, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, ⁴Department of Surgery, Faculty of Medicine and Health, Örebro University, Örebro, ⁵Department of Public Health and Clinical Medicine, Dermatology, Umeå, ⁶Department of Biomedical and Clinical Sciences, and Wallenberg Centre for Molecular Medicine, Linköping University, Linköping, ⁷Department of Surgery, Vrinnevi Hospital, Norrköping, ⁸Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, ⁹Department of Physiology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Studies of the effects of bariatric surgery on psoriasis are few, with conflicting results. By linking the Swedish **National Register for Systemic Treatment of Psoriasis** (PsoReg) with the Scandinavian Obesity Surgery Registry (SOReg), individuals with psoriasis who had undergone bariatric surgery in Sweden during 2008 to 2018 were identified, and matched with data for patients with psoriasis in PsoReg. Psoriasis Area Severity Index (PASI) and Dermatology Life Quality Index (DLQI) were compared between the groups. Altogether, 50 operated individuals (median body mass index (BMI) 38.7 kg/m²) and 91 non-operated individuals (median BMI 33.0 kg/m²) were included. Control of disease at baseline was good in both groups. Linear mixed models showed no significant difference in psoriasis disease burden, measured as changes in mean PASI (Δ PASI) (-1.2, p = 0.43) and DLQI (Δ DLQI) (-2.2, p = 0.34). In summary, this study demonstrated no significant effect of bariatric surgery on psoriasis disease burden in patients with relatively well-controlled moderate to severe psoriasis.

Key words: psoriasis; bariatric surgery; body mass index; Swedish National Register for Systemic Treatment of Psoriasis; Scandinavian Obesity Surgery Registry; Psoriasis Area Severity Index; Dermatology Life Quality Index; obesity.

Accepted May 5, 2021; Epub ahead of print May 6, 2021

Acta Derm Venereol 2021; 101: adv00487.

Corr: Marta Laskowski, Department of Dermatology and Venereology, Gröna stråket 16, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden. E-mail: marta.laskowski@vgregion.se

Psoriasis is a chronic, immune-mediated, inflammatory disease affecting the skin and other organs. There are different manifestations of psoriasis, among which plaque psoriasis is the most common (1), affecting up to 90% of patients with psoriasis (2). Psoriasis is classified as mild, moderate or severe. Conventional non-biologic systemic treatments and biologic therapies, targeting T-cell proliferation and the cytokines involved in psoriasis pathophysiology (2), are recommended for moderate to severe psoriasis (3, 4). Approximately 10–20% of patients with plaque psoriasis are in need of systemic therapy (2).

SIGNIFICANCE

Psoriasis is associated with increased risk of obesity. Bariatric surgery achieves long-term weight loss and reduces risks related to obesity. Both improvement and deterioration of psoriasis have been reported after bariatric surgery. We used Swedish nationwide quality registries for treatment of psoriasis and bariatric surgery to identify operated and non-operated psoriasis patients with obesity. The patients were matched and the effects of bariatric surgery on psoriasis disease burden were analysed and compared between the groups. Among patients with well-treated psoriasis, no evidence of either a beneficial or a negative effect of bariatric surgery on psoriasis was found.

There is a strong association between psoriasis and metabolic syndrome (5, 6), which is a cluster of metabolic disorders that also includes obesity (7). Metabolic syndrome is associated with increased levels of proinflammatory cytokines (8). There is a dose-dependent relationship between body mass index (BMI) and increased risk of psoriasis (9, 10), and psoriasis severity is correlated with increased risk for obesity (11).

Bariatric surgery has been shown to be superior to non-surgical weight loss interventions in achieving long-term weight loss. There are various types of bariatric surgical procedures, including Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy and gastric banding (12). Bariatric surgery leads not only to long-term weight loss, but, more importantly, to improvement in quality of life and reduction in the prevalence and severity of comorbidities and all-cause mortality. The mechanisms of action in bariatric surgery appear to be complex and include changes in gut hormones, bile acid metabolism and the gut microbiome (12).

The research investigating the effects of bariatric surgery on psoriasis is limited and publications largely include case reports (13, 14) and retrospective observational studies in small cohorts, mainly consisting of women and lacking control groups (15–17). Furthermore, the severity of psoriasis, in relation to post-surgical dermatological outcomes, has not been addressed in previous studies.

To the best of our knowledge, outcomes regarding both Psoriasis Area Severity Index (PASI) and Dermatology Life Quality Index (DLQI), post-bariatric surgery, have not been investigated previously. Some studies have indicated that bariatric surgery has a positive impact on psoriasis, with reduced psoriasis severity, resulting in reduction in psoriasis treatment, and improved quality of life (15–17). The positive effects have previously been linked to RYGB (15–18), as well as to higher age and absence of family history of psoriasis (16, 17). In addition, bariatric surgery was recently associated with a reduced risk of new-onset psoriasis (18, 19) and improved prognosis of psoriasis (18) in 2 large register-based studies. It is hypothesized that the positive effects of bariatric surgery on psoriasis are due to anti-inflammatory actions as a result of a complex neuro-hormonal interaction (20). However, exacerbations of psoriasis, post-bariatric surgery, have also been described (20–22).

This study aimed to investigate whether bariatric surgery, performed in patients with moderate to severe psoriasis, is associated with improvement or deterioration in psoriasis disease burden. Using Swedish nationwide registries for systemic treatment of psoriasis and bariatric surgery, this study identified operated patients with psoriasis and matched them with non-operated obese patients with psoriasis. This allowed us to longitudinally analyse the impact of bariatric surgery on moderate to severe psoriasis and evaluate whether bariatric surgery has an effect in addition to that offered by systemic treatments for psoriasis.

PATIENTS AND METHODS

The Swedish National Register for Systemic Treatment of Psoriasis and the Scandinavian Obesity Surgery Registry

The databases of the Swedish National Register for Systemic Treatment of Psoriasis (PsoReg) and the Scandinavian Obesity Surgery Registry (SOReg) were used to identify patients with moderate to severe psoriasis, who had had severe obesity and undergone bariatric surgery (hereinafter referred to as the "surgery group") and patients with obesity and moderate to severe psoriasis who had not undergone bariatric surgery (hereinafter referred to as the "control group").

Since its launch in 2006, the PsoReg has recorded data on patients of all ages with psoriasis who have received systemic therapy under specialized dermatological care in Sweden. The main intention is to follow the long-term safety and effectiveness of biologic treatments (23). The current coverage is 65% among those treated with biological agents (24). The register data are collected using tools such as the PASI (25, 26) and the DLQI (25, 27) and a wide range of variables including current systemic treatment, psoriasis subtype, and lifestyle factors, such as smoking and alcohol use, are also registered (28). In the present study, PASI and DLQI were used as outcome measures for psoriasis disease burden.

Since its establishment in its current form in 2007, the SOReg has been offering comprehensive nationwide follow-up data on bariatric surgeries performed in Sweden at all public and private hospitals, with a coverage exceeding 97%, and with > 99% correct data (29). The SOReg has been validated as a reliable source to identify patients who have undergone bariatric surgery (30).

Study population

The data in PsoReg and SOReg were linked using the 12-digit personal identification number allocated to all Swedish citizens. The linkage allowed the identification of all reported cases of moderate to severe psoriasis, based on their inclusion in PsoReg. with a history of bariatric surgery (n=172) during the follow-up period of 2007 to 2019 (Fig. 1). Bariatric surgery was performed during 2008 to 2018. Individuals with repeated bariatric surgery (n=3), individuals who were not registered in PsoReg pre- and post-bariatric surgery (n = 105), and individuals with missing data on PASI and DLQI pre- and post-bariatric surgery (n=10) were excluded from the analysis. Index dates in the surgery and control groups were the date of surgery and the median registration date in PsoReg, respectively. Two randomly selected patients with obesity (BMI > 30 kg/m²) from PsoReg were matched per case with respect to age (age at index ± 1 year), sex, and start of intervention (date of bariatric surgery ±1 year) among the 1,328 patients with

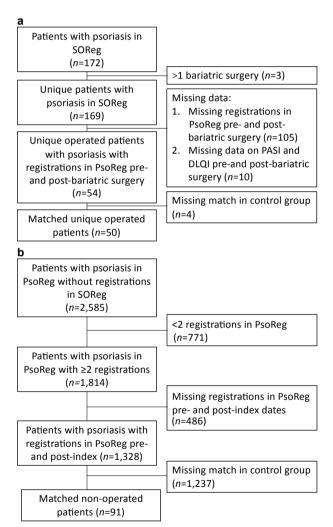


Fig. 1. Inclusion of individuals during follow-up (2007 to 2019). (a) Flowchart of included and excluded operated individuals, showing the number of cases of patients with moderate to severe psoriasis with a history of bariatric surgery (surgery group). Unique psoriasis patients are patients with history of no more than 1 bariatric surgery. (b) Flowchart of included and excluded non-operated individuals, showing the number of patients with moderate to severe psoriasis without a history of bariatric surgery (control group). DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area Severity Index; PsoReg: Swedish National Register for Systemic Treatment of Psoriasis; SOReg: Scandinavian Obesity Surgery Registry.

psoriasis who had at least one registration pre- and post-index, respectively, in PsoReg.

To avoid bias due to pre-surgical changes in psoriasis treatment, the registration in PsoReg closest to, but not before, 180 days preindex was used as baseline PASI and DLQI. The registration in PsoReg closest to, but not later than, 1 year after the index date was used as short-term follow-up. Later outcomes were analysed using the registration closest to, but not later than, 2 years from the index date (later follow-up).

No formal informed consent is needed for registration in Swedish registries. However, patients are informed about their inclusion and right to withdraw upon registration and can actively refrain from participating (i.e. by opting out). Informed consent was not required for inclusion in the current study as only pseudonymized data were used. The study was approved by the Regional Ethical Review Board in Gothenburg (DNR 656-17).

Statistical methods

Descriptive statistics are presented as medians with interquartile ranges (IOR) or frequencies and percentages. Linear mixed models were used to estimate the differences between the groups in PASI and DLQI post-baseline. The appropriate pre-baseline value was included in all the models. To account for matching, a random intercept was included for each matched set. When evaluating intergroup differences in changes in PASI (ΔPASI) and DLQI (ΔDLOI), the study corrected for potential confounders. All models included adjustments for baseline values of PASI and DLQI. Model 2 additionally adjusted for baseline BMI. Model 3 also included adjustments for known risk factors for psoriasis (smoking, amount and frequency of alcohol intake, and family history of psoriasis), psoriasis subtype (plaque psoriasis, nail psoriasis and other psoriasis), baseline treatment and psoriatic arthritis (PsoA). Two sub-analyses were performed, the first of which included only plaque psoriasis and the second including those who had undergone RYGB. Follow-up data are presented for individuals with matching BMI (±2 units). All statistical analyses were performed using SAS v 9.4 software (SAS Institute, Cary, NC, USA).

RESULTS

Table I shows the baseline characteristics of the study population. Altogether 50 operated cases and 91 matched individuals, randomly chosen from the 1,328 non-operated cases, were included based on the matching criteria. The median BMI was 5.7 units higher in the surgery group compared with the control group. Females constituted 60% of the surgery group and 57.1% of the control group. Plaque psoriasis was the most common subtype in both groups and most patients had had an onset of psoriasis at 21–30 years of age. Non-biologic systemic treatment was ongoing in 52% and 58.2% of the individuals in the surgery and control groups, respectively, while 36% and 28.6%, respectively, were receiving biologic systemic treatments. Table SI¹ shows details of the baseline treatments of the included individuals.

Roux-en-Y gastric bypass constituted 80% of the performed bariatric surgeries, while sleeve gastrectomy and gastric banding constituted 18% and 2%, respectively, of performed procedures (Table I).

The median time from baseline to surgery was 323 days (interquartile range (IQR) 243–516 days) for PASI values and 319 days (IQR 245–432 days) for DLQI values. **Table II** shows the follow-up data for the surgery and control groups. There was a large decrease in BMI (8.0 units) and body weight (28.5 kg) over time in the surgery group, compared with the control group.

Table I. Baseline characteristics of patients with moderate to severe psoriasis before undergoing bariatric surgery (surgery group), and matched patients not undergoing bariatric surgery (control group)

| Sex, n (%) 39 (42.9) Male 20 (40) 39 (42.9) Female 30 (60) 52 (57.1) Age, years, median (IQR) 44.2 (38.6-48.7) 44.3 (39. Body mass index, kg/m², median (IQR) 38.7 (35.9-42.5) 33.0 (31. PASI ^b , median (IQR) 5.3 (2.1-10.0) 4.6 (1.8- | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| Male 20 (40) 39 (42.9) Female 30 (60) 52 (57.1) Age, years, median (IQR) 44.2 (38.6-48.7) 44.3 (39. Body mass index, kg/m², median (IQR) 38.7 (35.9-42.5) 33.0 (31. | |
| Female 30 (60) 52 (57.1) Age, years, median (IQR) 44.2 (38.6-48.7) 44.3 (39. Body mass index, kg/m², median (IQR) ^a 38.7 (35.9-42.5) 33.0 (31. | |
| Age, years, median (IQR) 44.2 (38.6-48.7) 44.3 (39. Body mass index, kg/m², median (IQR) ^a 38.7 (35.9-42.5) 33.0 (31. | |
| Body mass index, kg/m^2 , median (IQR) ^a 38.7 (35.9–42.5) 33.0 (31. | |
| | |
| | |
| | |
| DLQI ^C , median (IQR) 1.0 (0.0–7.0) 4.0 (1.0– | 9.0) |
| Psoriasis type, n (%) | |
| Plaque 39 (79.6) 78 (85.7) | |
| Erythroderma 3 (6.1) 2 (2.2) | |
| Guttate 0 (0) 1 (1.1) | |
| Non-palmoplantar pustular 1 (2.0) 8 (8.8) | |
| General pustular $2 (4.1)$ $1 (1.1)$ | |
| Palmoplantar pustular 1 (2.0) 3 (3.3) | |
| Acrodermatitis $0 (0.0)$ $0 (0.0)$ | |
| Nail 9 (18.4) 20 (22.0) | |
| Psoriasis debut age, n (%) | |
| 0-5 years 0 (0.0) 2 (2.2) | |
| 6–10 years 7 (14) 7 (7.7) | |
| 11–15 years 9 (18.0) 17 (18.7) | |
| 16–20 years 10 (20) 12 (13.2) | |
| 21–30 years 15 (30) 29 (31.9) | |
| 31–40 years 5 (10) 15 (16.5) | |
| 41–50 years 3 (6) 6 (6.6) | |
| > 50 years 0 (0.0) 1 (1.1) | |
| Unknown 1 (2) 2 (2.2) | |
| Psoriatic arthritis, n (%) | |
| Ongoing 15 (30) 22 (24.2) | |
| Previous 7 (14) 5 (5.5) | |
| Never 22 (44) 41 (45.1) | |
| Status unknown 6 (12) 23 (25.3) | |
| Treatment, n (%) | |
| Non-biologic systemic treatment 26 (52.0) 53 (58.2) | |
| Biologic systemic treatment 18 (36.0) 26 (28.6) | |
| No treatment 6 (12.0) 12 (13.2) | |
| Smoking ^d , <i>n</i> (%) | |
| | |
| 1 (1) | |
| (), | |
| Never 21 (42.9) 53 (58.2) | |
| Status unknown 0 (0) 1 (1.1) | |
| Alcohol intake, glasses per week, n (%) | |
| 1-2 25 (50.0) 36 (39.6) | |
| 3-4 9 (18.0) 31 (34.1) | |
| 5-6 1 (2.0) 9 (9.9) | |
| 7-9 3 (6.0) 0 (0.0) | |
| >10 1 (2.0) 1 (1.1) | |
| Unknown 11 (22.0) 14 (15.4) | |
| Tobacco (snuff) use, n (%) | |
| Active 10 (20.0) 16 (17.6) | |
| Previous 2 (4.0) 4 (4.4) | |
| Never 37 (74.0) 70 (76.9) | |
| Unknown 1 (2.0) 1 (1.1) | |
| Type of bariatric surgery, n (%) | |
| Roux-en-Y gastric bypass 40 (80.0) | |
| Sleeve gastrectomy 9 (18.0) | |
| Gastric banding 1 (2.0) | |

^aFor the surgery group, n=46. ^bFor the surgery group, n=48. For the control group, n=88. ^cFor the surgery group, n=49. For the control group, n=89. ^dFor the surgery group, n=49.

¹https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3825

Table II. Baseline and follow-up data on obese patients with moderate to severe psoriasis who underwent bariatric surgery (surgery group), and matched patients without history of bariatric surgery (control group)

| | Surgery group | | | | | Control group | | | | | | |
|---------------------------------------|---------------------|----|---------------------------------|----|---------------------------------|---------------|--------------------|----|---------------------------------|----|---------------------------------|----|
| | Baseline | n | Follow-up >0 but ≤1 years | n | Follow-up ≥1 but ≤2 years | n | Baseline | n | Follow-up >0 but ≤1 years | n | Follow-up ≥1 but ≤2 years | n |
| BMI, kg/m ² , median (IQR) | 38.7 (35.9-42.5) | 46 | 32.2 (27.9-34.4) | 38 | 30.7 (26.0-33.4) | 28 | 33.0 (31.2-36.6) | 91 | 33.2 (31.4-36.7) | 84 | 34.1 (31.7-38.3) | 49 |
| Weight, kg, median (IQR) | 116.3 (101.0-131.0) | 48 | 94.5 82.0-112.0) | 38 | 87.8 (78.5-109.6) | 28 | 100.0 (93.0-108.0) | 91 | 100.1 (93.5-109.8) | 84 | 99.0 (87.0-107.5) | 49 |
| PASI, median (IQR) | 5.3 (2.1-10.0) | 48 | 5.6 (2.5-9.0) | 36 | 2.0 (0.9-7.2) | 28 | 4.6 (1.8-9.0) | 88 | 2.8 (1.2-6.0) | 77 | 2.6 (1.0-5.6) | 46 |
| DLQI, median (IQR) | 1.0 (0.0-7.0) | 49 | 2.0 (1.0-6.0) | 34 | 2.0 (1.0-3.0) | 26 | 4.0 (1.0-9.0) | 89 | 2.0 (1.0-8.0) | 84 | 2.0 (0.0-5.5) | 48 |
| Pso treatment, n (%) | | 50 | | 50 | | 50 | | 91 | | 91 | | 91 |
| No treatment | 6 (12.0) | | 15 (30.0) | | 25 (50.0) | | 12 (13.2) | | 11 (12.1) | | 44 (48.4) | |
| Non-biologic systemic | 26 (52.0) | | 26 (52.0) | | 17 (34.0) | | 53 (58.2) | | 51 (56.0) | | 23 (25.3) | |
| Biologic systemic | 18 (36.0) | | 9 (18.0) | | 8 (16.0) | | 26 (28.6) | | 29 (31.9) | | 24 (26.4) | |
| PsoA, n (%) | | 50 | | 38 | | 28 | | 91 | | 84 | | 49 |
| Ongoing | 15 (30.0) | | 11 (28.9) | | 6 (21.4) | | 22 (24.2) | | 21 (25.0) | | 15 (30.6) | |
| Previous | 7 (14.0) | | 6 (15.8) | | 6 (21.4) | | 5 (5.5) | | 3 (3.6) | | 1 (2.0) | |
| No | 22 (44.0) | | 16 (42.1) | | 14 (50.0) | | 41 (45.1) | | 41 (48.8) | | 22 (44.9) | |
| Unknown | 6 (12.0) | | 5 (13.2) | | 2 (7.1) | | 23 (25.3) | | 19 (22.6) | | 11 (22.4) | |

BMI: body mass index; IQR: interquartile range; DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area Severity Index; Pso: psoriasis; PsoA: psoriatic arthritis. n denotes 100% of participants in each category.

Both cohorts showed positive trends in PASI during follow-up (Table II). The median follow-up time from the index registration to short-term and later follow-up was 219 days (IQR 133–289) and 601 days (IQR 500–646), respectively, for PASI values in the surgery group, compared with 205 days (IQR 98-310) and 584 days (IQR 475–669) in the control group (data not shown). Fig. 2a presents the median PASI values at baseline, and at the short-term and the later follow-up, in the 2 groups. The follow-up data indicated small differences in changes in PASI (\triangle PASI) between groups. Therefore, the above hypothesis (see "Introduction") was tested by examining the mean $\triangle PASI$ in the 2 groups during the follow-up period. No statistically significant effect was detected for $\Delta PASI$, even when correcting for potential confounders (Table SII¹).

As both cohorts also showed positive trends in DLQI during follow-up (Table II, Fig. 2b), we compared the mean Δ DLQI between the 2 groups (Model 1, Table SII¹).

Even after correcting for potential confounders, no statistically significant effect was detected for $\Delta DLQI$ (Model 3, Table SII¹). The median follow-up time from the index registration to short-term and later follow-up was 231 days (IQR 133–289) and 601 days (IQR 528–638), respectively, for DLQI in the surgery group, compared with 209 days (IQR 94–311) and 597 days (IQR 494–673) in the control group.

Table SIII¹ presents follow-up data in patients with plaque psoriasis. In accordance with the results from the main cohort, no statistically significant difference between the groups was seen for $\Delta PASI$ and $\Delta DLQI$ (Table SIV¹).

A decreasing proportion of operated patients were treated with active biologic systemic treatment at short-term follow-up (from 36% to 18%), but this trend was not observed in the control group. At the longer-term follow-up, both groups showed a decrease in the proportion of patients with ongoing non-biologic systemic treatment

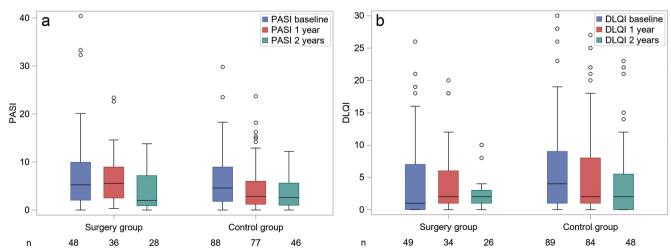


Fig. 2. (a) Psoriasis Area Severity Index (PASI) and (b) Dermatology Life Quality Index (DLQI) at baseline, and at the short-term and the longer-term follow-up, for patients with moderate to severe psoriasis with and without a history of bariatric surgery. The lines in the box-and-whiskers plots represent median values (50th percentile); the box spans the 25th–75th percentile; the lower whiskers denote the minimum values and the upper whiskers denote the 1.5 interquartile range (IQR). Values beyond the whiskers are marked with symbols and are considered as outliers.

(from 52% to 34% among operated vs 58.2% to 25.3% among non-operated patients) (Table II). Furthermore, there was a trend showing a decreasing proportion of patients with ongoing PsoA in the surgery group compared with an increase in the control group (Table II). In light of previous reports of beneficial effects of RYGB on plaque psoriasis (15–17), a sub-analysis of cases operated with RYGB was performed. This showed no additive effects on psoriasis outcomes in the RYGB-operated subgroup compared with the control group and the results were consistent when including only patients with plaque psoriasis (Table SV¹).

Table SVI¹ presents follow-up data in individuals with matching BMI (±2 units), showing that a larger proportion of patients who underwent surgery were treated with biologic systemic treatments at baseline compared with the main surgery cohort (46.7% and 36.0%, respectively). Furthermore, a larger proportion of the operated patients in the matched group had no ongoing systemic treatment at the later follow-up, compared with the main surgery cohort (73.3% and 50.0%, respectively).

DISCUSSION

This study investigated whether bariatric surgery had additive treatment effects on psoriasis disease burden in a population of patients with moderate to severe psoriasis. The main finding was that in relatively well-controlled patients with obesity and moderate to severe psoriasis, no clear effect of bariatric surgery on PASI and DLQI was seen, compared with a non-operated, matched control group. However, there was a decrease in systemic treatment, and for biological treatment, this occurred earlier in the surgery group.

Two retrospective chart studies, performed by Romero-Talamás et al. (16) and Hossler et al. (17), have indicated that psoriasis improvement, post-bariatric surgery, is limited to cases of RYGB among patients aged 45 years or older without heredity for psoriasis. In a large retrospective register-based cohort study, Egeberg et al. (18) showed that RYGB was also associated with a significant risk reduction of progression to severe psoriasis. A subanalysis of individuals in the current study population undergoing RYGB did not show any improvement in mean $\Delta PASI$ or $\Delta DLQI$ values compared with the control group (Table SV^1).

In the current study, 88% of the individuals were treated with systemic agents prior to bariatric surgery. Within the first year after surgery, a decrease was found in the proportion of operated patients requiring ongoing biologic systemic treatment (from 36% to 18%). This was in contrast to the control group, for whom an increase was noted (from 28.6% to 31.9%). However, at the later follow-up, fewer patients in both groups were receiving either non-biologic or biologic systemic treatment. We hypothesize that this could represent a sustained overall

decrease in disease activity among patients with psoriasis treated with systemic agents, which has been reported previously for biologic treatments (23). The trend showing early postoperative cessation of biologic agents in the surgery group may indicate an improvement in psoriasis severity, undetectable by $\Delta PASI$ and $\Delta DLQI$. This could support limited findings reporting that systemic therapies were frequently stopped after bariatric surgery (15).

The underlying mechanisms for the suggested positive effect of bariatric surgery on psoriasis are not fully understood, although anti-inflammatory mechanisms, including decreased cytokine levels, reduced leptin levels and increased levels of the gut incretin hormone glucagon-like peptide-1 (GLP-1), have been hypothesized (20). It is suggested that the absence of positive effects of bariatric surgery on PASI and DLOI in patients with moderate to severe psoriasis, seen in the current study, may reflect 2 phenomena. Firstly, the overall median PASI and DLQI at baseline in the current study were relatively low, which limited the detection of significant improvements of these parameters postbariatric surgery. Secondly, systemic medications may mask the anti-inflammatory and cytokine-inhibiting effects suggested to be induced by bariatric surgery. Consequently, this would provide support to the hypothesis that decreased cytokine activity constitutes an important mechanism for psoriasis improvement post-bariatric surgery (20).

Study strengths and limitations

The study design, including matched cohorts of men and women over a substantial time-period, as well as access to follow-up data, regarding both severity of cutaneous manifestations of psoriasis and dermatologyspecific quality of life, are strengths of this study. The high coverage (>97%) and validity of SOReg, with a very high accuracy of reported surgical procedures (30), is a further strength. Additional strengths of the study include access to the large number of variables in PsoReg and SOReg, which enabled the correction of known confounders for psoriasis outcomes, including treatment at baseline. Considering that the PsoReg is managed and designed by dermatologists in a specialist setting, the risk of misclassification of diagnoses should be very low. As plaque psoriasis constituted the majority of the cases of psoriasis in the current study, the use of the PASI and DLQI as outcome measures for psoriasis in PsoReg should be considered a further strength, as these are validated gold standard tools for assessing plaque psoriasis disease burden and health-related quality of life (25). To address the risk of bias resulting from PASI assessments on other subtypes of psoriasis, a sub-analysis was performed including only individuals with plague psoriasis, which showed results consistent with those from the main cohort (Table SIV1). Although the PASI

has been thoroughly validated and is considered the most valid and reproducible tool in the assessment of plaque psoriasis (25), intra- and inter-observer variations have been reported when assessing psoriasis severity using this tool (31).

A weakness of this study is the small sample size, which prevented us from stratifying by age. Therefore, positive effects of bariatric surgery on older age groups, which have been suggested in previous studies (16, 17), cannot be ruled out. Another limitation is the relatively low nationwide coverage of PsoReg (65% of biologic treatments), presenting a risk of bias due to missing data.

The difference in median BMI at baseline between the 2 groups is a further limitation of the study. BMI could not be included in the analyses as a matching variable because of the small sample size. However, follow-up data when matching for BMI (± 2 units) suggested that, compared with the main surgery cohort, there was a larger proportion of operated patients who were treated with a biologic systemic treatment at baseline (Tables II and SVI¹). Furthermore, there was a decrease in the proportion of operated patients with ongoing treatment at the later follow-up, which was largely due to cessation of biologic therapies. These results further support the limited previous findings that bariatric surgery leads to a cessation of systemic medications. However, the results of the current study are limited by the small sample size.

The absence of data on topical treatments and dosages of systemic medications are further limitations of the study. Furthermore, lifestyle changes during follow-up have not been taken into account, which could constitute risk of bias. Since this study had no access to data on physical activity and diet, it is not known whether the individuals in the control group underwent any weight loss interventions. However, there were no BMI changes that would suggest any successful weight loss interventions in the control group. While this study had no access to clinical data, the possibility of an impact on psoriasis status due to changes in medications or altered health status cannot be ruled out.

Conclusion

In summary, bariatric surgery has well-known and important implications in the treatment of severe obesity, leading to the resolution of comorbidities, and survival benefits. However, this study was unable to demonstrate a definite positive or negative effect on disease burden in a small cohort of patients with moderate to severe psoriasis with low baseline PASI and DLQI undergoing bariatric surgery, compared with matched controls. Future studies would be of interest, preferably prospective controlled trials including bariatric surgery in obese patients with psoriasis refractory to systemic treatment.

ACKNOWLEDGEMENTS

The authors would like to express our gratitude to the funding sources for this study.

This study was supported by grants from the Swedish Council for Working Life, Health, and Welfare (FORTE), and from the Swedish State under the ALF agreement between the Swedish Government and the County Councils (ALFGBG-74570), the Psoriasis Fund (Psoriasisfonden), the Sahlgrenska University Hospital Funds (SU-fonderna, SU-786171, SU-896101 and SU-935908), the Wilhelm and Martina Lundgren Science Fund (Wilhelm och Martina Lundgrens Vetenskapsfond, 2020-3371), and the Royal and Hvitfeldtska Foundation (Kungliga och Hvitfeldtska stiftelsen).

The funding sources had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, the preparation, review or approval of the manuscript, or the decision to submit the manuscript for publication.

The authors have no conflicts of interest to declare.

REFERENCES

- Schon MP, Boehncke WH. Psoriasis. N Engl J Med 2005; 352: 1899-1912.
- Sbidian E, Chaimani A, Afach S, Doney L, Dressler C, Hua C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev 2020; 1: CD011535.
- Mrowietz U, Kragballe K, Reich K, Spuls P, Griffiths CE, Nast A, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res 2011; 303: 1–10.
- Smith CH, Jabbar-Lopez ZK, Yiu ZZ, Bale T, Burden AD, Coates LC, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. Br J Dermatol 2017; 177: 628–636.
- Langan SM, Seminara NM, Shin DB, Troxel AB, Kimmel SE, Mehta NN, et al. Prevalence of metabolic syndrome in patients with psoriasis: a population-based study in the United Kingdom. J Invest Dermatol 2012; 132: 556–562.
- Cohen AD, Gilutz H, Henkin Y, Zahger D, Shapiro J, Bonneh DY, et al. Psoriasis and the metabolic syndrome. Acta Derm Venereol 2007; 87: 506–509.
- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365: 1415–1428.
- Sutherland JP, McKinley B, Eckel RH. The metabolic syndrome and inflammation. Metab Syndr Relat Disord 2004;
 82-104.
- Kumar S, Han J, Li T, Qureshi AA. Obesity, waist circumference, weight change and the risk of psoriasis in US women.
 J Eur Acad Dermatol Venereol 2013; 27: 1293–1298.
- Wolk K, Mallbris L, Larsson P, Rosenblad A, Vingard E, Stahle M. Excessive body weight and smoking associates with a high risk of onset of plaque psoriasis. Acta Derm Venereol 2009: 89: 492–497.
- Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and obesity: a systematic review and meta-analysis of observational studies. Nutr Diabetes 2012; 2: e54.
- 12. Wolfe BM, Kvach E, Eckel RH. Treatment of obesity: weight loss and bariatric surgery. Circ Res 2016; 118: 1844–1855.
- Higa-Sansone G, Szomstein S, Soto F, Brasecsco O, Cohen C, Rosenthal RJ. Psoriasis remission after laparoscopic Rouxen-Y gastric bypass for morbid obesity. Obes Surg 2004; 14: 1132–1134.
- de Menezes Ettinger JE, Azaro E, de Souza CA, dos Santos Filho PV, Mello CA, Neves M, Jr., et al. Remission of psoriasis after open gastric bypass. Obes Surg 2006; 16: 94–97.

- 15. Farias MM, Achurra P, Boza C, Vega A, de la Cruz C. Psoriasis following bariatric surgery: clinical evolution and impact on quality of life on 10 patients. Obes Surg 2012; 22: 877–880.
- Romero-Talamás H, Aminian A, Corcelles R, Fernandez AP, Schauer PR, Brethauer S. Psoriasis improvement after bariatric surgery. Surg Obes Relat Dis 2014; 10: 1155–1159.
- 17. Hossler EW, Wood GC, Still CD, Mowad CM, Maroon MS. The effect of weight loss surgery on the severity of psoriasis. Br J Dermatol 2013; 168: 660–661.
- Egeberg A, Sorensen JA, Gislason GH, Knop FK, Skov L. Incidence and prognosis of psoriasis and psoriatic arthritis in patients undergoing bariatric surgery. JAMA Surg 2017; 152: 344–349.
- Maglio C, Peltonen M, Rudin A, Carlsson LMS. Bariatric surgery and the incidence of psoriasis and psoriatic arthritis in the Swedish Obese Subjects Study. Obesity (Silver Spring) 2017: 25: 2068–2073.
- 20. Sako EY, Famenini S, Wu JJ. Bariatric surgery and psoriasis. J Am Acad Dermatol 2014; 70: 774–779.
- 21. Nowlin N, Solomon H. Letter: Weight loss and psoriasis. Arch Dermatol 1976; 112: 1465.
- 22. Perez-Perez L, Állegue F, Caeiro JL, Zulaica JM. Severe psoriasis, morbid obesity and bariatric surgery. Clin Exp Dermatol 2009; 34: e421–422.
- 23. Hjalte F, Carlsson KS, Schmitt-Egenolf M. Sustained Psoriasis Area and Severity Index, Dermatology Life Quality Index and EuroQol-5D response of biological treatment in psoriasis: 10 years of real-world data in the Swedish National Psoriasis

- Register. Br J Dermatol 2018; 178: 245-252.
- 24. Nationella kvalitetsregistret för systembehandling av psoriasis. Psoreg:s årsrapport för 2018. 2018.
- Paul C, Gourraud PA, Bronsard V, Prey S, Puzenat E, Aractingi S, et al. Evidence-based recommendations to assess psoriasis severity: systematic literature review and expert opinion of a panel of dermatologists. J Eur Acad Dermatol Venereol 2010; 24: 2-9.
- 26. Fredriksson T, Pettersson U. Severe psoriasis oral therapy with a new retinoid. Dermatologica 1978; 157: 238–244.
- Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19: 210–216.
- Schmitt-Egenolf M. PsoReg the Swedish registry for systemic psoriasis treatment. The registry's design and objectives. Dermatology 2007; 214: 112–117.
- Sundbom M, Naslund I, Naslund E, Ottosson J. High acquisition rate and internal validity in the Scandinavian Obesity Surgery Registry. Surg Obes Relat Dis 2020; 10.1016/j. soard.2020.10.017.
- Tao W, Holmberg D, Naslund E, Naslund I, Mattsson F, Lagergren J, et al. Validation of Obesity Surgery Data in the Swedish National Patient Registry and Scandinavian Obesity Registry (SOReg). Obes Surg 2016; 26: 1750–1756.
- 31. Puzenat E, Bronsard V, Prey S, Gourraud PA, Aractingi S, Bagot M, et al. What are the best outcome measures for assessing plaque psoriasis severity? A systematic review of the literature. J Eur Acad Dermatol Venereol 2010; 24: 10–16.