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Maintenance of quality of life improvement for patients with chronic pain and obesity after interdisciplinary multimodal pain rehabilitation – a study using the Swedish Quality Registry for Pain Rehabilitation (SQRP)

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Significance: Patients with chronic pain and comorbid obesity achieve sustained improvements in Health-Related Quality of Life (HRQoL) from Interdisciplinary Multimodal Pain Rehabilitation (IMMPR). This finding suggests that rehabilitation professionals should consider using IMMPR for patients with comorbid obesity even though their improvement may not reach the same level as for non-obese patients.

Abstract

Background: Throughout the world many people have both obesity and chronic pain, comorbidities that decrease Health-Related Quality of Life (HRQoL). It is uncertain whether patients with comorbid obesity can maintain improved HRQoL after Interdisciplinary Multimodal Pain Rehabilitation (IMMPR).

Methods: Data from 2016, 2017, and 2018 were obtained from a national pain database for Swedish specialized pain clinics and collected at three time points: Pre-IMMPR; Post-IMMPR; and 12-month follow-up (FU-IMMPR). Participants (N=872) reported body weight, height, pain aspects, and HRQoL (RAND 36-Item Health Survey). Severe obesity (Body Mass Index, BMI $\geq$35 kg/m^2) was defined according to WHO classifications. We used linear mixed regression models to examine BMI group differences in HRQoL over time.

Results: More than 25% of patients (224/872) were obese and nearly 30% (63/224) of these were severely obese. All BMI groups improved significantly in both physical and mental composites of HRQoL after IMMPR (Pre- vs. Post-IMMPR, P<0.001). The improvements were maintained at a 12-month follow-up (Post- vs. FU-IMMPR, P>0.05). The severe obesity group had the lowest physical health score and least improvement (pre- vs. FU-IMMPR, Cohen's d= 0.422, small effect size). Severe obesity had negative impact on physical health (β=-4.39, P<0.05) after controlling for sociodemographic factors and pain aspects.

Conclusion: Improvements in HRQoL after IMMPR were achieved and maintained across all weights, including patients with comorbid obesity. Only severe obesity was negatively associated with physical health aspects of HRQoL.

Significance: Patients with chronic pain and comorbid obesity achieve sustained Health-Related Quality of Life (HRQoL) improvements from Interdisciplinary Multimodal Pain Rehabilitation (IMMPR). This finding suggests that rehabilitation professionals should consider using IMMPR for patients with comorbid obesity even though their improvement may not reach the same level as for non-obese patients.

Introduction

Obesity and chronic pain are common comorbidities that often lead to hardships (Cooper, Ells, Ryan, & Martin, 2018; Hitt, McMillen, Thornton-Neaves, Koch, & Cosby, 2007; Marcus, 2004; Narouze & Souzdalnitski, 2015; Okifuji & Hare, 2015; Stone & Broderick, 2012). More than 50% of the European population is overweight or obese (Marques, Peralta, Naia, Loureiro, & de Matos, 2018), resulting in substantial economic burdens for patients and society (Phillips, 2009; Tremmel, Gerdtham, Nilsson, & Saha, 2017), and 20% of Europeans report chronic pain of at least moderate intensity(Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006).

Although the causal obesity-pain relationship has not been fully explored, evidence suggests that obesity and pain adversely affect one another as they share underlying mechanical, physiological, psychological, and behavioural mechanisms (McVinnie, 2013; Okifuji & Hare, 2015; Zdziarski, Wasser, & Vincent, 2015).

Quantitative and qualitative research have tried to identify barriers to treating the two comorbidities. For example, Arranz et al. describe the relationship between obesity and pain as a vicious circle that challenges rehabilitation efforts: pain-inactivity-obesity-pain (Arranz, Rafecas, & Alegre, 2014). In another qualitative study, Cooper et al. found that 'overweight/obesity contributed to fear and catastrophizing, which resulted in avoidance of exercise that would have assisted their weight loss' (Cooper, Ells, et al., 2018). As these insights suggest, providing pain rehabilitation to patients across all the weight classes and expecting similar results will be challenging.

According to the VAPAIN initiative, Health-Related Quality of Life (HRQoL) is one of the main outcome domains in Interdisciplinary Multimodal Pain Rehabilitation (IMMPR) (Kaiser et al., 2018). Prior studies have linked HRQoL both with obesity and pain (Arranz et al., 2014; Barofsky, Fontaine, & Cheskin, 1997; Heo, Allison, Faith, Zhu, & Fontaine, 2003). This association is not a direct linear correlation, but a result of accumulated effects when obesity and pain coexist. In other words, individuals with the two comorbidities may have worse HRQoL compared to patients with only one of the two conditions. Given that these two comorbidities affect HRQoL simultaneously, we asked whether focus only on pain management is sufficient for improving HRQoL in obese patients.

As the comorbidity of obesity and pain is prevalent (Hitt et al., 2007; Narouze & Souzdalnitski, 2015), pain rehabilitation considers weight status. There is some indication that patients benefit from IMMPR irrespective of weight status across BMI classes (Castel et

al., 2015; Koball, Craner, & Sperry, 2016). However, Koball et al.'s study (Koball et al., 2016) did not investigate the sustainable improvements at follow-up and Castel et al.'s study (Castel et al., 2015) included only female fibromyalgia patients. Therefore, this study aims to investigate chronic pain patients in real-world practice settings registered in the SQRP with respect to the following research questions:

Is obesity overrepresented in patients referred to specialist pain clinics in Sweden?

In comparison to normal weight patients, do patients with obesity report more severe pain?

Is obesity an obstacle factor for chronic pain patients to improve HRQoL and maintain improvements after IMMPR?

Which factors influence HRQoL maintenance over time?

Methods

The Swedish Quality Registry for Pain Rehabilitation (SQRP)

Recognized by the Swedish Association of Local Authorities and Regions, the Swedish Quality Registry for Pain Rehabilitation (SQRP) receives data from pain clinics at the specialist level throughout Sweden. In 2010, The Boston Consulting Group ranked SQRP as one of the top ten high-quality national registries in Sweden ("Boston Consulting Group," 2010). SQRP uses questionnaires to capture patients' sociodemographic background, pain characteristics, psychological symptoms, function, activity/participation aspects, and HRQoL. Previous publications provide a more detailed description of these variables (Gerdle, Molander, Stenberg, Stalnacke, & Enthoven, 2016). In 2016, two variables – self-reported body weight and height – were added to the SQRP. Patients complete the SQRP questionnaires on up to three occasions: during the first physician visit (Pre-IMMPR or baseline); immediately after IMMPR (Post-IMMPR); and at a 12-month follow-up after IMMPR (FU-IMMPR). In this study, we extracted data from two consecutive years, between 2016 and 2018, so as to cover IMMPR participants from pre-IMMPR through FU-IMMPR.

Participants

For this study, patients were asked to participate in the SQRP after being referred to a specialized pain clinic due to complex chronic non-malignant pain conditions. A bio-psycho-social assessment revealed that these patients presented psychological symptoms and other comorbidities, reported large difficulties with their pain, and their condition severely affected their working life and participation in social activities. In addition, they often did not respond to routine pharmacological/physiotherapeutic treatments delivered in a monodisciplinary fashion. Exclusion criteria were substance abuse and ongoing major somatic or psychiatric disease. The participants (N=872) were ≥18 year, registered in the SQRP, completed selected measurements (described below), treated with the IMMPR, and completed the SQRP at all three occasions (Pre-IMMPR, Post-IMMPR, and FU-IMMPR).

The study was conducted in accordance with the Helsinki Declaration and Good Clinical Practice and approved by the Ethical Review Board in Linköping (Dnr: 2015/108-31). All participants received written information about SQRP research and gave their written consent.

Measurements

Sociodemographic characteristics

Data collected included age, sex, educational level, place of birth, and working status. Educational level was classified as follows: elementary school, upper secondary school or

vocational training, and college or university. Place of birth was categorised as Sweden, another Nordic country, Europe except Nordic country, or country outside Europe. Before IMMPR and at the follow-up, participants were asked about their occupation: working status (employed or self-employed), studies, or neither. This variable was dichotomised into working/studying and not working/studying.

Pain aspects
Pain intensity (NRS-7d) was defined as average pain intensity during the previous week using a numeric rating scale 0-10 with numbers for guidance 0 = no pain and 10 = worst possible pain). Minimal clinically important difference (Cook, 2008) for pain is considered as a change of pain intensity of at least 30% (Farrar, Young, LaMoreaux, Werth, & Poole, 2001).

Pain duration was determined by asking a single question: When did you first experience the pain you are currently troubled by (days)?

Pain-duration-persistent was determined by asking a single question: If persistent pain exists, how long (days)?

Pain distribution (Pain Region Index, PRI) was determined using 36 predefined anatomical areas (18 on the front and 18 on the back of the body). The participants marked where they experienced pain: 1) head/face, 2) neck, 3) shoulder, 4) upper arm, 5) elbow, 6) forearm, 7) hand, 8) anterior aspect of chest, 9) lateral aspect of chest, 10) belly, 11) sexual organs, 12) upper back, 13) low back, 14) hip/gluteal area, 15) thigh, 16) knee, 17) shank, and 18) foot. The number of areas with pain were summed (i.e., between 0 and 36) and this created a Pain Region Index (PRI) for the participants.

Anthropometric variables
Information on height and weight were self-reported or measured and registered during the clinical assessment. BMI (kg/m^2) was calculated as weight (kg)/height (m)^2 and classified according to the World Health Organization (WHO) criteria: <18.5 = underweight; 18.5-24.9 = normal range; 25.0-29.9 = overweight; 30.0-34.9 = obesity; and ≥35.0 = severe obesity.

The validity of measured weight- and height-calculated BMI and BMI derived from self-reported values have previously been investigated. High correlations were reported between the two measures (Pearson's r = 0.89-0.97 for different age groups and gender) (Kuczmarski, Kuczmarski, & Najjar, 2001). Based on the measured BMI, self-reported values (sensitivity

of 88.1% and specificity of 97.4%) are used to identify overweight/obesity (Vuksanović et al., 2014).

Psychological symptoms

A self-assessment questionnaire was used to measure anxiety and depression – Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). HADS is devided into an anxiety subscale (HAD-A) and a depression subscale (HAD-D). Both subscales have seven items, scoring range between 0 and 21, where a lower score indicates a lower possibility of anxiety or depression. HADS is frequently used in clinical practice as well as in research and has good psychometric characteristics (Bjelland, Dahl, Haug, & Neckelmann, 2002; Zigmond & Snaith, 1983). HADS has the following clinical cut-offs: 0-7 = no symptoms; 8-10 = probably symptomatic; and ≥11= severely symptomatic (Zigmond & Snaith, 1983). A cut-off value of ≥11 for severe symptomatology was used to define the minimal clinically important difference after IMMPR. HADS has been validated in its Swedish translation (Lisspers, Nygren, & Soderman, 1997).

HRQoL

RAND-36 is one of the generic profile HRQoL measures used to compare the relative burden of chronic disease (Hays & Morales, 2001; Hays, Sherbourne, & Mazel, 1993). Comprising 36 items, RAND-36 assesses eight health dimensions with multi-item scales, including physical functioning (10 items), role limitations caused by physical health problems (4 items), role limitations caused by emotional problems (3 items), social functioning (2 items), emotional wellbeing (5 items), energy/fatigue (4 items), pain (2 items), and general health perceptions (5 items). In addition, one item assesses change in perceived health during the previous 12 months. In each health dimension, every term is transformed linearly to a 0-100 possible range (per cent of total possible score) and then total score averages are calculated in the same scale. This calculation yields eight scale scores (ranging 0-100). Two summary scores, physical and mental health composites (PCS and MCS), were also derived from these eight scales. We used the two summaries in this study.

Statistical analysis

All statistics were performed using the statistical package IBM SPSS Statistics (version 23.0). Data are presented as means with standard deviation (SD) for variables with normal distribution and medians with interquartile range (IQR) for variables with non-Gaussian distribution. SQRP uses predetermined rules to handle single missing items of a scale or a subscale; details about this procedure are reported elsewhere (Gerdle et al., 2016). To

investigate differences among the groups with different BMI categories, we used Chi-square, one-way ANOVA (Bonferroni method for post hoc test), and Kruskal-Wallis Test (Mann-Whitney U test with Bonferroni method for post hoc test). A p-value of below 0.05 was regarded as statistically significant. A P-value < 0.017 was used for Mann-Whitney U test, which served as a post hoc test to control for the risk of mass significance (Altman, 1991). To investigate within group changes at the one-year follow-up, we used paired sample t-test and calculated effect size (ES, Cohen's $d=t/\sqrt{N}$) (Lakens, 2013) to quantify the differences between Pre-IMMPR and FU-IMMPR. The effect size (Cohen's d) was considered large if ≥0.80, moderate if 0.50-0.79, small if 0.20-0.49, and insignificant if <0.20 (Cohen, 1988).

To avoid likewise deletion of missing data in repeated measures ANOVA, we structured linear mixed models to analyse repeated measures at three time points: Pre-IMMPR, Post-IMMPR, and FU-IMMPR. The models can also deal with time-varying covariates. Two summary scores of HRQoL measured on the three IMMPR occasions, PCS and MCS, served as dependent variables. Time (Pre-, Post-, and FU-IMMPR) was a repeated measure and treated as a categorical variable. To investigate the possible effect modifications with time and BMI group (TIME x BMI group), this interaction term was specified in all the models. The change in BMI (as a time-varying variable) was calculated by subtracting the BMI at Pre-IMMPR from the BMI at FU-IMMPR. BMI directly after IMMPR (Post-IMMPR) was assumed as unchanged. In model 1, only BMI group, change in BMI, time, and its interaction with BMI group were tested. In model 2, sociodemographic characteristics (working/study status as a time-varying variable) were added. In model 3, pain aspects (pain intensity as a time-varying variable) and psychological symptoms (HADs as time-varying variables) were added. Collinearity was prior tested and two variables – pain duration and pain-duration-persistent – had a high correlation of 0.764. Pain-duration-persistent was removed from the models due to more missing data than that in pain duration. A repeated covariance type with unstructured statement fitted best (according to Akaike's information criterion) to account for correlations on an individual level between the repeated measures at baseline and the other two IMMPR occasions. Analysis was conducted using maximum likelihood estimation since our sample is not small (Singer & Willett, 2003). The regression coefficients (β) and standard error (SE) were generated in the regression models. F-statistic were reported when appropriate.

Results

Sociodemographic characteristics

Table 1 summarises the sociodemographic characteristics. Most chronic pain patients were middle aged (45.8±10.5 years old), women (n=700, 80%), Swedish or European (n=778, 89.5%), and without college or university education (628/872, 72%). The proportion of work/study status increased at follow-up (Pre-IMMPR vs. FU-IMMPR, 57% to 73.9%, P<0.001).

More than one-fourth (224/872, 25.6%) of the study population was categorised as obese. Nearly one-third of the obese patients (63/224, 28.1%) were severely obese. Mean BMI did not change over the time (Pre- vs. FU-IMMPR, P>0.05). Due to the low representation of underweight participants (12/872, 1.4%), this category was not considered in the later analysis.

Table 1 to be here.

Pain aspects, psychological symptom, and HRQoL

Obese patients reported longer pain duration than normal-weighted patients with respect to days since chronic pain debut and persistent pain duration (Table 2). Obese patients also had more pain spreading based on PRI (17 vs. 13, P<0.001). Pain intensity (NRS-7d) differed most significantly among the BMI groups at FU-IMMPR. At FU-IMMPR, the mild obesity group (6.2±2.3) and the severe obesity group (6.4±2.0) reported higher pain intensity than the normal weight group (5.4±2.3, P<0.001). Although significant decreases of pain intensity were found in all groups (Pre- vs. FU-IMMPR, Cohen's d 0.328~ 0.453, small ES, all p<0.05) except for the overweight group (Pre- vs. FU-IMMPR), the changes were not clinically important (i.e., a decrease of at least 30%).

Reported psychological symptoms measured by HADS did not differ statistically between weight groups at any of the three IMMPR measurements (Table 2). Significantly lower scores in all the groups were reported at follow-up (Pre- vs. FU-IMMPR, Cohen's d 0.363~0.524, small to moderate ES, all P<0.01). A further analysis of HADS score below clinical cut-off showed that fewer patients were included in the category 'severely symptomatic' (Pre- vs. FU-IMMPR, P<0.001, data not shown), indicating that improvement was of clinical importance.

Table 2 to be here.

All BMI groups showed significant improvements in the two composites of HRQoL (PCS and MCS) after IMMPR (Pre- vs Post-IMMPR, all P< 0.001, Figures 1 and 2). The improvements were stable and maintained at the follow-up (Pre- vs. FU- IMMPR, Cohen's d 0.328 ~ 0.579, small to moderate ES, all P<0.05; Post- vs. FU-IMMPR, all P>0.05). The severe obesity group had the lowest PCS and the least improvement (Pre- vs FU-IMMPR, Cohen's d = 0.422, small ES, P<0.01) (Figure 1). The other three groups with lower BMI had greater improvements (Cohen's d >0.5, moderate ES, all P<0.001). MCS did not show group differences at any of the three time points. The improvement in MCS after IMMPR was also rather limited in each group (mean difference 6.5~ 11.5, Cohen's d < 0.5, small ES). The group with severe obesity had the least improvement in MCS among the BMI groups (Pre- vs. FU-IMMPR, Cohen's d = 0.328, small ES, P<0.05).

Figure 1 and figure 2 to be here.

Mixed linear regression of PCS and MCS
Coefficients of variables selected to determine the relationship with PCS or MCS changing over time (Pre-, Post-, and FU-IMMPR) are shown in Table 3. When only the BMI group was considered, time (Pre-, Post-, and FU-IMMPR), change in BMI, and time-BMI group interaction (BMI group x time) were part of the analysis. BMI group (F (3, 845) = 6.559, P<0.01) with mild obesity (β = -5.59, P<0.01) and severe obesity (β = -10.34, P<0.01) contributed negatively to PCS, but had no significant effect on MCS (model 1, Table 3). After adjusting for background factors, the significant impacts of BMI group on PCS remained (model 2, Table 3). For severe obesity, its significant negative effect also remained when pain aspects and psychological symptoms were added (β =-4.39, P<0.05, model 3 in Table 3). For group difference over time, time-BMI group interaction did not show significant impact on PCS (F (6, 799) = 0.80, P>0.05) or MCS (F (6, 770) = 1.025, P>0.05, model 1 in Table 3); the insignificant effect remained in the other two models.

Among the sociodemographic factors in model 2 and model 3, work or study remained as a positive effect on both PCS (β =1.8-3.36, P<0.01) and MCS (β =1.6-5.7, P<0.05). As expected, some variables also showed robust impacts on PCS and MCS (i.e., pain intensity and pain distribution, HADS-A (only upon MCS), and HADS-D).

Table 3 to be here.

Discussion

The results of our study confirm that obesity is common among patients with chronic pain. In this study, over 25% of patients referred to Swedish specialist pain clinics were obese. This is a higher proportion than that reported in the overall Swedish population (approximately 15%) (Sweden, 2018). In this study, obese patients reported longer duration of chronic pain, more widespread pain (PRI), and higher pain intensity, supporting the notion that obese chronic pain patients experience more severe pain than non-obese chronic pain patients. We found that IMMPR benefited patients across all the weight groups from normal weight through obesity with regard to improvements in HRQoL at discharge and at one-year follow-up. However, severely obese patients reported the least improvements in HRQoL after IMMPR, and severe obesity was negatively related to physical health over time. Finally, clinically important improvements after IMMPR were found for psychological symptoms, but not for pain intensity.

A further investigation on pain aspects showed that pain intensity, often considered to correlate with low HRQoL (Bernfort, Gerdle, Rahmqvist, Husberg, & Levin, 2015; Breivik et al., 2006; Dysvik, Lindstrom, Eikeland, & Natvig, 2004; Horng et al., 2005), only showed minor variations across the weight groups at Pre-IMMPR. Obese patients are known to experience lower HRQoL than other patients (Jia & Lubetkin, 2005; Marcus, 2004; Simon et al., 2006), but our results indicate that before IMMPR patients were referred to specialist pain clinics they experienced similar levels of pain intensity regardless of weight group. Although obese patients had the least reduced pain intensity Post-IMMPR, no BMI group reported a reduction large enough to reach the minimal clinically important difference. Consistent with our findings, two other research groups focused on morbidly obese patients receiving weight loss interventions, also reported lack of clinically significant reduction in pain intensity (Cooper, Ryan, et al., 2018; Dunlevy et al., 2019). In the normal weight group, the effect size was small, but this must be seen in the perspective that these patients represent a selection of patients with complex chronic pain conditions. So far, we cannot blame excess weight as a major independent barrier in pain intensity reduction. Based on the present results, we cannot assume that changes in BMI per se will result in pain intensity reduction by IMMPR. As other studies have suggested, IMMPR's goal should not be the significant reduction of pain intensity (Bromley Milton et al., 2013; Gerdle et al., 2016; Turk et al., 2008; Turk & Okifuji, 1999).

Obese patients are known to experience more psychological symptoms than other patients (Jia & Lubetkin, 2005; Marcus, 2004; Simon et al., 2006). In our study population, under the condition that patients are simultaneously suffering chronic pain, weight status seemed less significant in affecting psychological wellness. No statistically significant differences were found in HAD-A, HAD-D, or the mental aspect of HRQoL (as measured by MCS) between weight groups (Table 2 and Figure 2). Also, in the regression models, BMI could not explain the variation in MCS. Previous research, including our recent studies, have shown increased prevalence of psychological distress in complex chronic pain conditions and positive correlations between pain intensity and levels of psychological distress in these patients (Borsbo, Peolsson, & Gerdle, 2009; Chopra & Arora, 2014; Molander, Dong, Ang, Enthoven, & Gerdle, 2018; Nicolson, Caplan, Williams, & Stern, 2009). Hence, we may speculate that factors other than obesity status dominate or expand the negative influence on patients' mental wellness in complex chronic pain conditions.

Return to meaningful activity, such as work or study, can be a main objective for rehabilitation, since the majority of patients referred to IMMPR are of working age. From the regressions of both composites of HRQoL, it was evident that only work/study status was a significant regressor (Table 3). There are several reports, including longitudinal studies, that have found that more patients return to work and achieve better HRQoL after IMMPR (Chu et al., 2015; Hallstam, Lofgren, Svensen, & Stalnacke, 2016; Rivano Fischer, Persson, Stalnacke, Schult, & Lofgren, 2019; Westman et al., 2006). Our results clearly indicate that the two aspects of HRQoL investigated here had a positive influence on work/study status.

Both pain aspects and psychological symptoms were important variables associated with patients' HRQoL according to the regression models (model 3 of PCS and MCS) (Table 3). Based on estimates of coefficients in the models, our results indicate that pain aspects had stronger effects on physical health HRQoL (measured by PCS), whereas psychological symptoms were more important for mental health HRQoL (measured by MCS). During IMMPR, PCS compared to MCS was more improved and the effect maintained over time when Pre-, Post-, and FU-IMMPR were considered. In rehabilitation, maintenance of improved outcomes is very important because it represents both long-term effects of pain rehabilitation and cost-effective treatment (i.e., reduced medical care) (Sletten, Kurklinsky, Chinburapa, & Ghazi, 2015) and return to work (Norrefalk, Ekholm, Linder, Borg, & Ekholm, 2008).

The obesity epidemic continues in Sweden as well as around the world. In pain rehabilitation, weight status is receiving more attention (Koball et al., 2016; Marcus, 2004; Sellinger et al., 2010). There are concerns that the negative health consequences of obesity may restrict the pain rehabilitation process. However, our study supports studies that conclude that patients with different weight status benefit equally from IMMPR (Castel et al., 2015; Koball et al., 2016; Sellinger et al., 2010). The fact that we have used follow-up IMMPR data and found maintenance effects on HRQoL, clearly indicates that health professionals should offer IMMPR to patients regardless of weight status. However, our most complex model (model 3 in Table 3) of PCS indicates that severe obesity might be a barrier. To some extent, obesity seemed to negatively affect pain intensity (Table 2). On the other hand, having severe pain can be a barrier to weight loss for obese patients receiving weight management services (Masheb et al., 2015; Ryan et al., 2017). Both conditions, severe pain and extreme obesity, interfere with patients' attempts to improve in one or the other condition. The complex interwoven relationship suggested here reminds health professionals about the underlying mechanisms (McVinnie, 2013) and the necessity of targeting pain rehabilitation and weight management in an integrated fashion (Dunlevy et al., 2019; Janke et al., 2014).

This study has several limitations. First, we did not analyse IMMPR for non-participants or drop-outs. It remains unclear whether excess weight is an obstacle for patients and health care professionals when considering IMMPR after clinical assessment. We did not have enough information about obesity-related health problems that could have contributed to non-participation or drop-outs. Because the conclusions of this study are based on a population referred to tertiary care for pain rehabilitation that completed IMMPR and follow-up registrations, the generalizability of our findings are limited. Second, because we did not consider other obesity comorbidities, we may be neglecting the multi-morbidity influence on outcomes of pain rehabilitation. Our earlier research showed that certain comorbidities play an important role in older patients (Dong, Larsson, Levin, Bernfort, & Gerdle, 2018). However, IMMPR participants in Sweden are usually of working ages and one of the main IMMPR's goals is return to work/study (Gerdle et al., 2016). Third, we paid most attention to HRQoL, one of several outcome domains in IMMPR, to analyse whether weight status affects HRQoL. Thus, the positive conclusion of benefits from IMMPR with respect to PCS and MCS regardless of excess weight cannot simply be extended to other outcomes. Future studies should explore other outcome domains of IMMPR, especially from the perspective of patients with severe obesity.

Conclusion

We observed improved HRQoL from IMMPR applied to patients with a BMI range from normal weight to obesity. This finding suggests that rehabilitation professionals should consider using IMMPR for patients with comorbid obesity, even though their progress may not be as great as non-obese patients. This study showed that only severe obesity was negatively associated with physical health aspects of HRQoL (PCS) after IMMPR when important aspects of the clinical presentation such as pain intensity, spreading of pain, and psychological distress were considered.

Acknowledgement

Authors' contributions

All authors contributed to the conception of the study. HJD analysed the data in close

collaboration with BG. HJD drafted the manuscript. All the authors commented on different

versions of the manuscript and all the authors approved the final version of the manuscript.

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Legends for illustrations and tables

Table 1. Sociodemographic characteristics of the study population.

Table 2. Comparisons among BMI categories.

Figure 1. Rand 36 Physical Component Summary (PCS).

Figure 2. Rand 36 Mental Component Summary (MCS).

Table 3. Linear mixed regression.

Table 1. Sociodemographic characteristics of the study population.

IMMPR participants, N=872	n (%)
Age (years), mean±SD [a]	45.8 ± 10.5
Female gender	700 (80.3)
Birth of place [b]	
Sweden	732 (83.9)
Another country in Europe	46 (5.3)
Outside of Europe	91 (10.4)
Highest education, college/university	244 (28.0)
Current working or studying	
Pre-IMMPR	474 (57.4)
FU-IMMPR	644 (73.9)[d]
Body Mass index (BMI), mean±SD	
Pre-IMMPR	27.45±5.18
FU-IMMPR [c]	27.33±4.99[e]
BMI group	12 (1.4)
Underweight	12 (1.4)
Normal weight	280 (32.1)
Overweight	356 (40.8)
Mild obese	161 (18.5)
Severely obese	63 (7.2)

Missing data: [a]=5, [b]=3, [c]=108;

Pre- vs. FU-IMMPR: [d] Chi-square, P<0.001; [e] Paired t test, *P*=0.599

Table 2. Comparisons among BMI categories.

	Normal weight N= 280	Overweight N=356	Mild obesity N=161	Severe obesity N=63	P-value
Pain aspects					
Pain duration, days, median (q1-q3)	1755 (824-4146)	1969 (922-4948)	2772 (914-6708)[ae]	3752 (1108-7254)[be]	0.01
Pain-persistent- duration, days, median (q1-q3)	1160 (511-2644)	1311 (616-3719)	1832 (737-6035)[ae]	1884 (620-6502)	0.008
PRI, Mean±SD	13±8	15±8	17±8[ad]	17±9[bc]	<0.001
NRS-7d, Mean ± SD					
Pre-IMMPR	6.5±1.9	6.6±1.8	6.9±1.7	7.0±1.6	0.045
Post-IMMPR	5.4±2.4	5.3±2.3	5.7±2.1	5.9±2.1	0.081
FU-IMMPR	5.4±2.3	6.8±2.3	6.2±2.3[ad]	6.4±2.0[bd]	<0.001
Absolute Cohen's d (Pre- vs FU-IMMPR)	0.453	0.332	0.346	0.328	
Psychological symptoms					
HADS-A, Mean ± SD					
Pre-IMMPR	9.3±4.5	9.2±4.5	9.1±4.5	9.2±5.1	0.95
Post-IMMPR	7.5±4.2	7.6±4.4	7.6±4.4	7.8±4.9	0.959
FU- IMMPR	7.5±4.2	7.5±4.4	7.6±4.7	7.8±4.7	0.963
Cohen's d (Pre- vs FU-IMMPR)	0.444	0.429	0.385	0.363	-

HADS-D, Mean ± SD					
Pre-IMMPR	8.3±4.1	8.7±4.2	9.3±4.2	9.1±4.1	0.079
Post-IMMPR	6.1±4.0	6.7±3.9	6.8±4.1	6.2±3.7	0.17
FU-IMMPR	6.5±4.4	6.9±4.2	7.0±4.7	7.3±4.5	0.496
Cohen's d (Pre- vs FU-IMMPR)	0.430	0.460	0.524	0.426	-

Post-hoc: [a] mild obesity vs. normal weight significant, [b] severe obesity vs. normal weight significant; [c] $P<0.05$, [d] $P<0.01$ (ANOVA, Bonferroni method), [e] $P<0.017$ (Mann–Whitney U test, Bonferroni method). Cohen's d for effect size: large (d≥0.80), moderate (d=0.50-0.79), small (d=0.20-0.49), and insignificant (d<0.20).
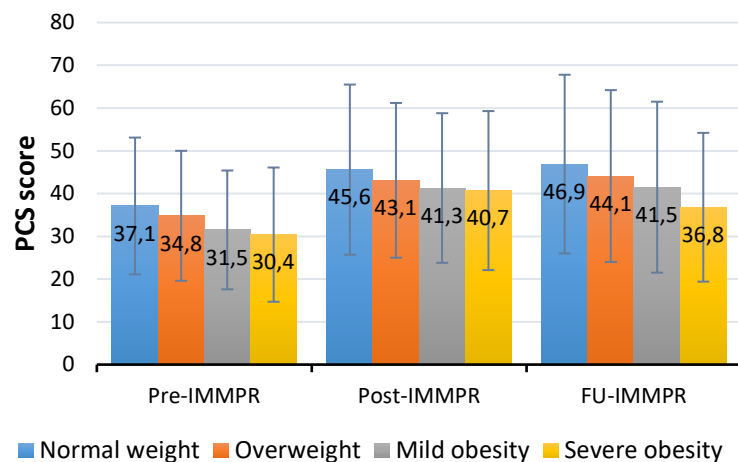

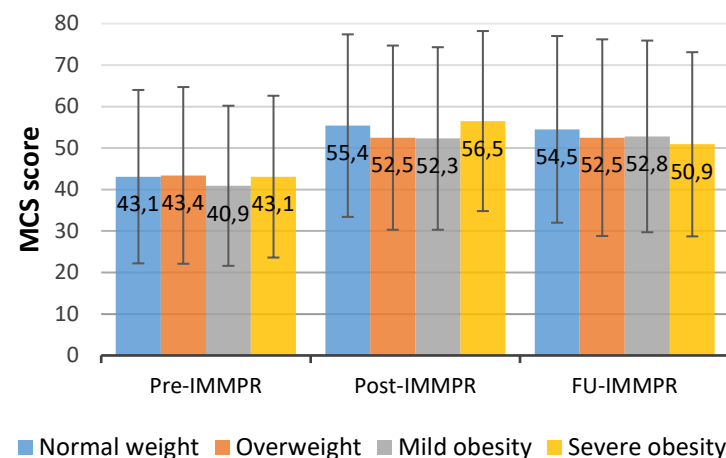Figure 1. Rand 36 Physical Component Summary (PCS)

Figure 2. Rand 36 Mental Component Summary (MCS)

Table 3. Linear mixed regression.

Estimate (SE)	Dependent variable: PCS			Dependent variable: MCS		
Predictors	Model 1 (n=852)	Model 2 (n=847)	Model 3 (n=779)	Model 1 (n=850)	Model 2 (n=845)	Model 3 (n=776)
Time, reference FU-IMMPR						NS
Pre-IMMPR	-9.90 (1.08)[b]	-9.22 (1.09)[b]	-3.78 (0.96)[b]	-10.85 (1.44)[b]	-9.69 (1.46)[b]	-
Post-IMMPR	-1.05 (1.03)	-1.05 (1.05)	-2.36 (0.97)[a]	1.21 (1.32)	1.32 (1.35)	-
BMI group, (reference normal weight)				NS	NS	NS
Overweight	-2.77 (1.64)	-2.31 (1.63)	0.26 (1.19)	-	-	-
Mild obesity	-5.59 (2.04)[b]	-5.43 (2.00)[b]	0.06 (1.47)	-	-	-
Severe obesity	-10.34 (2.89)[b]	-9.46 (2.83)[b]	-4.39 (2.10)[a]	-	-	-
University/college	-	3.24 (1.11)[b]	NS	-	NS	-
Male gender	-	3.04 (1.25)[a]	NS	-	4.32 (1.52)[b]	-
Work/study	-	3.36 (0.71)[b]	1.80 (0.63)[b]	-	5.70 (0.96)[b]	1.60 (0.70)[a]
Born in Sweden	-	5.07 (1.38)[b]	NS	-	9.62 (1.70)[b]	
NRS-7d	-	-	-3.29 (0.15)[b]	-	-	-1.31 (0.17)[b]
PRI	-	-	-0.33 (0.05)[a]	-	-	-0.17 (0.05)[b]
HADS-A	-	-	NS	-	-	-1.44 (0.11)[b]
HADS-D	-	-	-1.20 (0.09)[b]	-	-	-2.53 (0.10)[b]
Change in BMI	NS	NS	NS	NS	NS	NS
BMI x time	NS	NS	NS	NS	NS	NS

Model 1: BMI, time, change in BMI and BMI x time were tested; Model 2: sociodemographic variables were added; Model 3: pain aspects and psychological symptoms were added; [a] $P<0.05$, [b] $P<0.01$, *NS*: non significance.