ISSN: 2785-7263 DOI: 10.54103/dn/20383

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Systematic Review and Meta-Analysis

Preoperative biofeedback improves continence recovery after open prostatectomy: a systematic review and meta-analysis

Stefano Terzoni[1], Mauro Parozzi[1], Bernardo Rocco[2], Chiara Sighinolfi[3], Giorgia Gaia[3], Laura Di Prisco[1], Lara Carelli[1], Roberta Lodini[1], Elena Sala[1], Agostino D'Antuono[1], Cristina Mora[3], Serena Maruccia[3], Paolo Ferrara[1]

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Findings:

Preoperative biofeedback seems to lead to improved urinary continence after open prostatectomy.

ABSTRACT

BACKGROUND: Postoperative urinary incontinence is the overall result of urethral sphincter incompetence and modifications in urethral length after radical prostatectomy. Findings for preoperative interventions targeted at preventing post-prostatectomy incontinence include preoperative pelvic floor muscle training (PFMT) and biodfeedback (BFB), which can be managed by nurses in many countries and have been used for decades to speed up continence recovery after surgery.

AIM: We investigated the indications provided by the literature regarding preoperative biofeedback for preventing urinary incontinence after open radical prostatectomy, in terms of treatment regimens, timing for beginning the sessions, number of contraction and relaxation exercises, and scheduled work at home. We aimed to determine the effectiveness of preoperative biofeedback (BFB) for post-prostatectomy urinary incontinence compared to pelvic training without BFB, considering the variability between the results of the available studies.

METHODS: A systematic review and meta-analysis was conducted. Literature search on Pubmed, CINAHL, Cochrane Library, Web of Science, Scopus, EMBASE, and PEdro.

RESULTS: Despite only three papers being suitable for metanalysis, our results support BFB over written instructions for continence recovery after both 3 and 6 moths from surgery. Implementing progressive programs with many different muscular exercises and including relaxation are the main recommendations.

CONCLUSIONS: Preoperative biofeedback leads to improved urinary continence after 3 and 6 months from radical prostatectomy. Future studies should focus on the characteristics and number of pelvic muscle contractions required during biofeedback in order to maximize effectiveness.

KEYWORDS: *Pelvic Floor; Open Prostatectomy; Urinary Incontinence; Rehabilitation Nursing*

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Milano University Press

Submission received: 23/06/2023
End of Peer Review process: 28/07/2023
Accepted: 30/07/2023

ISSN: 2785-7263 DOI: 10.54103/dn/20383

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Journal Homepage: https://riviste.unimi.it/index.php/dissertationnursing

Revisione sistematica e Metanalisi

Il biofeedback preoperatorio migliora il recupero della continenza a seguito di prostatectomia radicale: una revisione sistematica e meta-analisi

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Riscontri:

Il biofeedback preoperatorio sembra migliorare la continenza urinaria dopo prostatectomia radicale.

ABSTRACT

INTRODUZIONE: L'incontinenza urinaria postoperatoria è il risultato complessivo dell'incompetenza dello sfintere uretrale e delle modifiche della lunghezza dell'uretra dopo la prostatectomia radicale. I risultati degli interventi preoperatori mirati a prevenire l'incontinenza post-prostatectomia includono l'allenamento preoperatorio dei muscoli del pavimento pelvico (PFMT) ed il biodfeedback (BFB), che possono essere gestiti dal personale infermieristico in molti Paesi e sono stati utilizzati per decenni per accelerare il recupero della continenza dopo l'intervento.

OBIETTIVO: sono state analizzate le indicazioni fornite dalla letteratura sul biofeedback preoperatorio per la prevenzione dell'incontinenza urinaria dopo la prostatectomia radicale aperta, in termini di regimi di trattamento, tempi di inizio delle sessioni, numero di esercizi di contrazione e rilassamento e lavoro programmato a casa. Il nostro obiettivo è stato quello di determinare l'efficacia del biofeedback preoperatorio (BFB) per l'incontinenza urinaria post-prostatectomia rispetto al training pelvico senza BFB, considerando la variabilità dei risultati degli studi disponibili.

METODI: È stata condotta una revisione sistematica con meta-analisi. La ricerca della letteratura è stata effettuata su Pubmed, CINAHL, Cochrane Library, Web of Science, Scopus, EMBASE e PEdro.

RISULTATI: Nonostante solo tre articoli fossero adatti alla metanalisi, i nostri risultati supportano il BFB rispetto alle istruzioni scritte per il recupero della continenza dopo 3 e 6 mesi dall'intervento. L'implementazione di programmi progressivi con molti esercizi muscolari differenti e l'inclusione del rilassamento sono le principali raccomandazioni.

CONCLUSIONI: Il biofeedback preoperatorio porta a un miglioramento della continenza urinaria dopo 3 e 6 mesi dalla prostatectomia radicale. Gli studi futuri dovrebbero concentrarsi sulle caratteristiche e sul numero di contrazioni muscolari pelviche richieste durante il biofeedback per massimizzare l'efficacia.

KEYWORDS: *Pavimento Pelvico; Prostatectomia Radicale; Incontinenza Urinaria; Infermieristica Riabilitativa*

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Submission received: 23/06/2023
End of Peer Review process: 28/07/2023
Accepted: 30/07/2023

Milano University Press

ISSN: 2785-7263 DOI: 10.54103/dn/20383

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BACKGROUND

Prostate cancer is the most common form of malignant neoplasm in men aged 50 or more [1] and radical prostatectomy (RP) is the first-choice surgical treatment for organ-limited prostate cancer, according to the European guidelines with over 90% of 15-year disease-specific survival [1]. Urinary incontinence is a common complication of RP, with prevalence ranging in literature from 4-8% to 59-63% [1] depending on the surgical technique, definition of continence chosen, measurement techniques for quantifying actual leakages, and follow-up timing.

Continence is the result of a complex mechanism of muscles working together: the proximal urethral sphincter, the levator ani muscular group and the rhabdosphincter all contribute to urinary control, all regulated by complex neurophysiological mechanisms [2]. Radical prostatectomy damages several of the structures that contribute to continence: the proximal sphincter is almost completely removed, so that postoperative continence mainly depends on the rhabdosphincter which can get damaged as well, due to his proximity to the prostate. Some authors have shown that up to 92% of patients with post-prostatectomy incontinence have autonomic denervation of the urethral mucosa, which suggests that the nervous bundle of the rhabdosphincter, more than the sphincter itself, is the crucial point [3]. Postoperative urinary incontinence is the overall result of urethral sphincter incompetence and modifications in urethral length. Urodynamic testing by urethral pressure profilometry shows that maximum urethral closure pressure is reduced by a median of 41% after radical retropubic prostatectomy (RRP) [4]. Furthermore, being the bladder affected by the surgical operation as well, patients can experience consequences on detrusor innervation and function [5] although there is little agreement in literature about this finding. Detrusor overactivity has been reported as an independent predictor of postoperative incontinence in men [6].

Over the past decade, findings for preoperative interventions targeted at preventing post-prostatectomy incontinence ("prehabilitation") have become available in the literature [7]. Such interventions include preoperative pelvic floor muscle training (PFMT) and biodfeedback (BFB) [7] which can be managed by nurses in many countries and have been used for decades to speed up continence recovery after surgery. PFMT consists of voluntary contractions of the *levator ani* muscle, aimed at improving strength and endurance of the pubocyccigeal muscle, which can help urethral closure if properly trained. BFB consists in the elecromyographical detection of pelvic muscles contraction, by using surface electrodes or rectal probes connected to a computer. It is widely used for teaching patients the correct way of contracting pelvic muscles during PFMT [8]. Almost all BFB machines allow the operator to choose between simply visualizing the electrical potential generated by muscular contraction and preparing a programme of "obstacles" with precise shape, heigth, and length. Obstacles are depicted on screen by the computer and can have different shapes such as triangular or square. Each shape requires the patient to perform a specific type of contraction: for example, to overcome a triangle-shaped obstacle, the patient needs to perform a fast contraction and release. Any contraction causes an increase of the electromiographic line on screen, due to the increase in the electrical potential during contractions. Therefore, it is possible to check if the patient is correctly activating the pelvic muscles, by simply verifying if the electromiographic line follows the shape of the obstacle. This allows precise tuning of pelvic training, because the characteristics of the obstacles require the patient to contract phasic and tonic fibers with specific criteria of intensity, duration, and number of repetitions, thus increasing strength, endurance, and resistance.

Two old meta-analyses by Wang et al. [7] and Chang et al. [8] have studied the role of preoperative PFMT; in some of the studies they considered, BFB had been used as a prehabilitation method, but the metanalyses did not make a distinction between PFMT alone and PFMT+BFB. While Wang and colleagues found no conclusive evidence about PFMT before open prostatectomy, Chang and colleagues included new studies in their paper, in addition to those considered by Wang et al., and found that preoperative PFMT improved postoperative urinary incontinence by 36% at three months (OR=.64, 95%CI[.47-.88]) but not at six months. Another metanalysis has been published in 2021 [9] which however did not add any significant information about biofeedback compared to the previous two. To date, the work by Chang et al. appears to be the most complete investigation

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Milano University Press

Submission received: 23/06/2023
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of this topic. However, some of the papers in the meta-analysis only studied PFMT alone, while others have used BFB in addition to PFMT compared to written instructions on how to perform pelvic training; furthermore, several comparisons were performed by the authors of the primary papers, as some used written or vebal instructions on how to perform PFMT as control. Some of the papers included in the meta-analysis have recommended preoperative biofeedback [10–12] while others have not [13,14]. Considering that BFB is a treatment requiring a dedicated machine, a trained professional, and a rectal probe that can be discomfortable for patients, it would be interesting to know whether adding BFB to PFMT leads to any improvement of postoperative continence compared to written instructions provided to patients, as done in several of the papers included in the existing metanalyses. Cheng and colleagues have not performed this type of comparison. Furthermore, recent literature [15,16] has shown a strong the relationship between the characteristics of exercise regimens (and therefore the methods used for teaching them) and the results: for this reason, the fact that BFB is always useful for teaching PFMT should not be taken for granted, nor should it be considered obvious that, if preoperative PFMT is useful, BFB will give good results as well.

The available evidence regarding prehabilitation with BFB only regards open prostatectomy; several trials are available, all suggesting different prehabilitation regimens and achieving different results. Notwithstanding the spreading of robot-assisted and minimally-invasive technologies, open techniques are still largely used (especially in centres which, due to the low volume of surgery performed, would not be able to economically sustain the costs of robotic surgery) as testified by the numerous papers published in recent years about the chracterics of this approach [17] and its consequences on urinary continence [18], these latter being matter of investigation in a systematic review [19]. This poses a rationale for conducting a metanalysis of studies regarding open techniques in 2020.

Overall, additional research is required to clarify the role of preoperative biofeedback and the characteristics it should have to grant continence in the long run. Long-term continence is obviously of great interest for patients and for healthcare providers, as relapses on incontinence are sometimes possible [16] and therefore it is interesting to study the longest possible follow-up periods.

Aims

To update and summarize the evidence regarding preoperative BFB for reducing post-prostatectomy urinary incontinence; to provide practical indication regarding the characteristics of the treatment that proved useful in relevant literature.

METHODS:

Design

We conducted a systematic review of the literature according to the methodology described by Palmer and Sterne [20]. The PICO question (Patients, Intervention, Control, Outcome) was: P=patients undergoing radical prostatectomy, I=preoperative BFB supervised by a trained professional, C=PFMT, O=postoperative urinary incontinence". An additional relevant question was "What are the indications provided by the literature regarding preoperative biofeedback for preventing urinary incontinence after radical prostatectomy, in terms of treatment regimens, timing for beginning the sessions, number of contraction and relaxation exercises, and scheduled work at home?"

PubMed, CINAHL, The Cochrane Library, SCOPUS, EMBASE, and Web of Science were searched with the keywords *preoperative, prostatectomy, "urinary incontinence", prevention, exercise, "pelvic floor muscle training", biofeedback*. Whenever possible, thesaurus keywords were used. Paper sources such as monographies, printed journals and scientific books were searched as well, by accessing the academic library of our teaching hospital. The literature search was stopped on April 15, 2022; this search was registered on XXX *(concealed for blinded review)* with a publicly accessible protocol. This study had no funding source and the authors did not have any competing interest.

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Submission received: 23/06/2023
End of Peer Review process: 28/07/2023
Accepted: 30/07/2023
Milano University Press

ISSN: 2785-7263 DOI: 10.54103/dn/20383

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Inclusion criteria

We included interventional studies published since 2000, considering that the very first papers on preoperative biofeedback were published in the early 2000s. The included studies we analyzed have enroled patients of all ages undergoing radical prostatectomy (any technique) for prostate cancer staged ≤ T_3, which according to the TNM staging (Tumour, lymhNodes, Metastatis) corresponds to intracapsular tumour [1]. Interventions had to involve preoperative PFMT with biofeedback (auditory, visual, or tactile). Studies of which the full text could not be retrieved were excluded. We relied on the university library for retrieving the highest possible number of full text papers. The flow of studies selection was reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement [21].

Study assessment

The characteristics of the studies were assessed by two authors using the PEDRO (Physiotherapy Evidence Database) scale [22] which has been expressely created for rehabilitation studies; the Rayyan platform was used to allow independent judgement of the papers by the two authors.

Statistical analysis

The analysis was carried out using the log odds ratio as the outcome measure, which was postoperative continence. A random-effects model was fitted to the data. The amount of heterogeneity (i.e., tau²), was estimated using the restricted maximum-likelihood estimator. In addition to the estimate of tau², the Q-test for heterogeneity and the I^2 statistic were reported. In case any amount of heterogeneity is detected (i.e., tau² > 0, regardless of the results of the Q-test), a prediction interval for the true outcomes was also provided. Studentized residuals and Cook's distances were used to examine whether studies may be outliers and/or influential in the context of the model. Studies with a studentized residual larger than the 100 x (1 - 0.05/(2 X k))th percentile of a standard normal distribution were considered potential outliers (i.e., using a Bonferroni correction with two-sided alpha = 0.05 for k studies included in the meta-analysis). Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances were considered influential. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor, were used to check for funnel plot asymmetry and subsequent risk of publication bias. To allow easier quantification of the clinical advantage obtained with BFB, odds ratios were calculated byexponential transformation of the original log odds ratios, and presented in the forest plots reported in this paper.

All calculations were performed with STATA® 17 for MacOS (StataCorp, Inc.).

RESULTS

We retrieved a total of 238 papers, 135 of which were excluded after reading the abstracts. Of the 73 remaining, 68 were excluded after reading the full text because they were duplicates or failed to fulfill the required design or enrolment criteria. Finally, 5 trials were included in this review (10–14). Figure 1 shows the flowchart of literature selection. All studies were compliant with the items of the PEDRO scale, apart for blinding which in this review was inappropriate due to the nature of treatments. Notwithstanding this positive methodological characteristic, the papers showed differences regarding the definition of continence chosen by the authors, the characteristics of the biofeedback programs, and the timing of interventions and follow-up. Similarly to Chang et al. (2015) we chose continence as the outcome of our analysis, defined as the absence of involuntary leakages [23]. Only one study [10] underwent power analysis. Some had very small sample size [12]; in most papers, no information regarding effect size of the intervention was included. Only one paper [24] enrolled patients undergoing laparoscopic prostatectomy; no studies on robotic surgery was found.

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Submission received: 23/06/2023
End of Peer Review process: 28/07/2023
Accepted: 30/07/2023

Milano University Press

ISSN: 2785-7263 DOI: 10.54103/dn/20383

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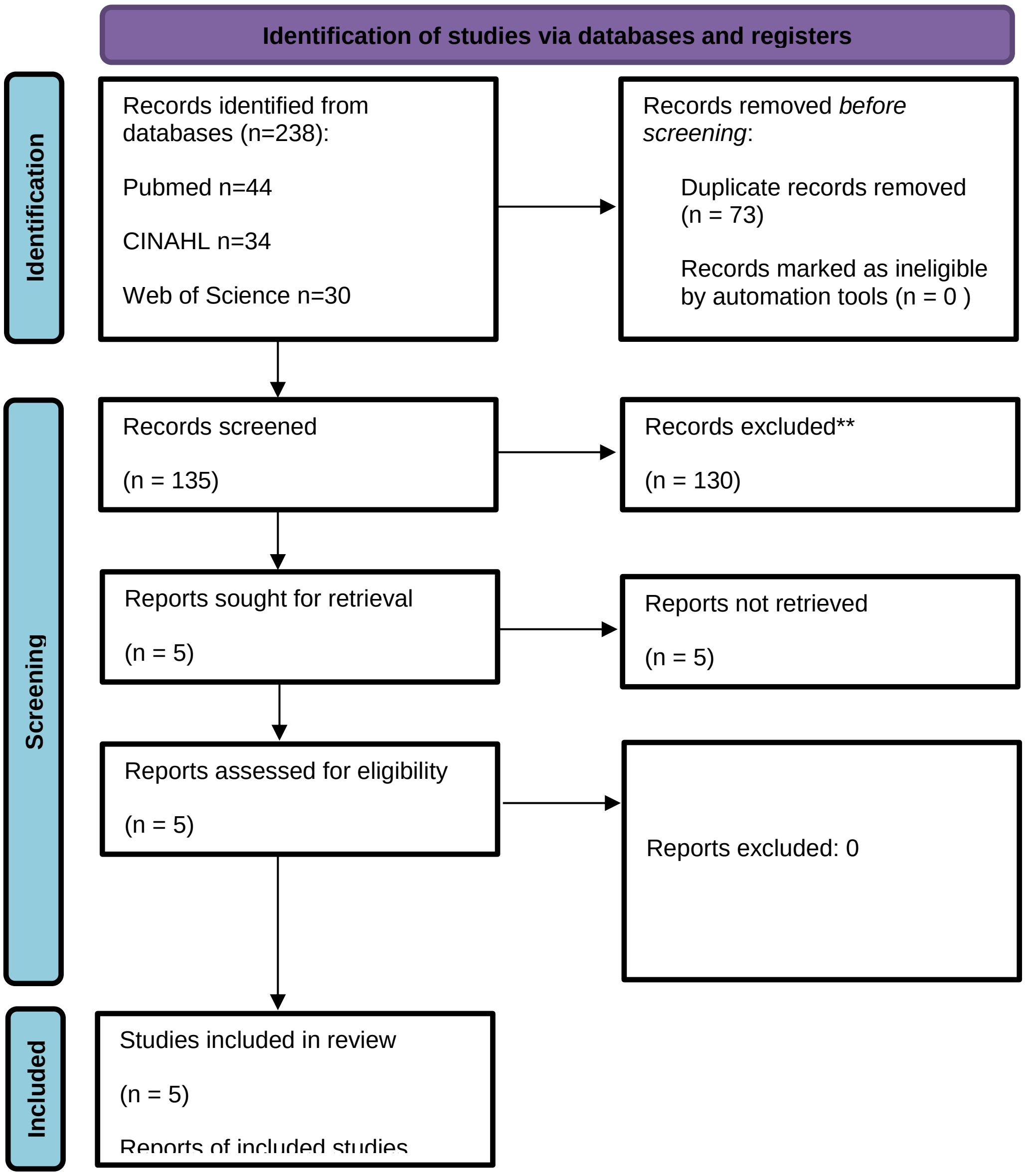

Figure 1: PRISMA flow diagram of literature search

Characteristics and results of preoperative feedback

Table 1 summarizes the characteristics of the studies and the criteria suggested by the authors for preoperative BFB. The total number of subjects was 406 (206 in the BFB group, 200 undergoing PFMT alone). Considerable clinical discrepancies were found between the papers in terms biofeedback methods (e.g. electromyographic vs barometric), control groups (e.g. pelvic floor exercises vs written instruction only) and follow-up criteria. Considering the small overall number of available studies and therefore the relevance of any information retrievable in the papers, we report a qualitative discussion of all papers prior to performing the metanalysis.

Burgio and colleagues [10] enroled 125 men undergoing radical prostatectomy, stratified according to tumor differentiation (Stage T_2a and T_2b). Bladder diaries, severe/continual leakage, daily pad count and Incontinence Impact Questionnaire were used as measures of outcome. The proportion with several/ continual

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Submission received: 23/06/2023
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Accepted: 30/07/2023

leakage at 6th month was statistically significant (5.9% group vs 19.6% group, p=.04.)

Article	Design	Intervention group size	Control Group size	Intervention details	Comparison	Power analysis
Bales, 2000	RCT	47	50	45 min BFB 2 to 4 weeks before surgery, 5-10", 10 to 15 repetitions.	Written instruction on postoperative PFMT	No
Burgio, 2006	RCT	50	46	1 session of BFB with 2 to 10" contraction and 2 to 10" relaxation of pelvic muscles + written instructions on 45 exercises (3 groups of 15) with 10" contractions in various positions and daily practice.	Postoperative instructions to interrupt the urinary flow	Yes
Collado Serra, 2013	RCT	35	43	3 weekly sessions of BFB + transversus abdominis activation in abdominal hypopressive technique + daily PFMT at home	Verbal instructions about Kegel's exercises afte surgery	No
De Lira, 2019	RCT	16	15	2 sessions of electromyographic BFB guided by a physiotherapist + instructions on how to continue PFMT postoperatively	Usual care (no prehabilitation)	No
Dijkstra, 2013	RCT	58	45	10 maximum force contractions of 3" + 3 maximum endurance contractions of 30" + 1 Valsalva + 1 min rest. Toilet training, abdominal breathing, muscle relaxation exercises.	7 days of postoperative PFMT alone	No
Lilli, 2006	Quasi experimental	45	45	PFMT + BFB two weeks before surgery, continued postoperatively	PFMT alone	No
Perez, 2018	Quasi experimental	20	32	Barometric BFB: 10 sessions, 7+6 min each (unspecified timing)	No treatment	No
Tienforti, 2012	RCT	16	116	1 day before surgery: 3 sessions/day of BFB, 10 minutes, 5" contraction + 5" relaxation, supine, repeated postoperatively after catheter removal.	No PFMT	No

Table 1: Characteristics of the studies

Another RCT [12] enrolled 32 patients undergoing open retropubic RP and found statistically significant differences at 1 month (p=.02), 3 month (p=.01) and 6 month follow up (p=.002). In intervention group continence had been achived by 6,8 and ten patients vs no patients, one patient and one patient in control group (p=.02; p=.01; p=.002).

Bales and and colleagues (Bales at al., 2000) enroled 100 men undergoing radical retropubic prostatectomy (RRP) and found no statistically significant differences between recovery rates in the two groups at 6 month follow up, since incidence of urinary continence was 94% vs 96% (p= .59)

Dijkstra-Eshuis and colleagues [24] enroled 122 patients undergoing laparoscopy-assisted radical prostatectomy (LARP) in a randomized clinical trial (RCT). All patients were assessed preoperatively by a physiotherapist. The intervention consisted of weekly 30-minutes sessions of PFMT for 4 weeks, with additional BFB according to a

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Milano University Press

ISSN: 2785-7263 DOI: 10.54103/dn/20383

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standardized protocol (no details provided) for improving endurance, muscular relaxation, and coordination with abdominal breathing. The patients were thought to perform the exercises in different positions (not specified) and to integrate them into daily activities. Control patients received written PFMT instruction after catheter removal. The authors performed interim analysis on 122 patients, as 224 would have been required to achieve 80% statistical power, but the study was closed in advance due to the lack of clinically relevant results: the treatment group had no advantages in terms of continence after 6 weeks, 3 months, 6 months, 9 months, and 12 months (p>.05 for all comparisons).

Collado et al. [11] analyzed data from 179 patients and found statistically significant differences in continence improvement, assessed with the International Consultation on Incontinence Questionnaire – Short Form (ICIQ-UI SF) at 6 weeks, 3 months, 6 months and one year after surgery (p=.03, .002, .009, and .03 respectively).

The study by Perez et al. [25] was excluded because it did not report follow-up timings; two other RCTs (26,27) was also excluded because the treatment programme included both pre- and postoperative BFB. At the end of the selection process, the only studies that could be included in the metanalyis were those comparing preoperative BFB with instructions on how to perform PFMT. Some studies had multiple follow-up times, but most included assessment at three and six months after surgery; we chose these timings for our analyses. The only exception was the study by Dijkstra-Eshuis [24] in which the number of months at which the authors conducted their the interim analysis was not specified. This study was not included in the quantitative synthesis, being the only one with PFMT as controls.

At the end of study selection, three papers showed comparable clinical characteristics [28–30]. Two of them suggested statistically significant improvement of continence with BFB [28,29] even though one reported enormous expected variability in the population [28]. A third study [30] did not find a statistically significant advantage attributable to BFB; this conflict among the papers suggested to proceed with a metanalysis.

Quantitative synthesis

Continence recovery – 3 months after surgery

Three studies were included. The observed log odds ratios ranged from 0.8591 to 2.7081, with most estimates being positive (100%). The estimated average log odds ratio was 1.0914 (95% CI[0.5230-1.6598]) and the average outcome differed significantly from zero ($z = 3.7635$, $p = 0.0002$). There was no significant amount of heterogeneity in the true outcomes ($Q[2] = 2.2295$, $p = 0.3280$, $tau^2 = 0.0000$, $I^2 = 0.0017\%$). The 95% prediction interval for the true outcomes was [0.5230- 1.6599]; therefore the true outcomes of the studies are generally in the same direction as the estimated average outcome. None of the studies had studentized residuals larger than ± 2.3940, suggesting the absence of outliers. According to the Cook's distances, none of the studies could be considered overly influential. The rank correlation test indicated no funnel plot asymmetry ($p = 0.1804$). Figure 2 shows the forest plot summarizing these findings, after exponential transformation to obtain odds ratios for clearer understanding of the effect size.

Continence recovery – 6 months after surgery

Three studies were included. The observed log odds ratios ranged from 0.6329 to 3.2189, with most estimates being positive (100%). The estimated average log odds ratio was 1.5440 (95% CI[0.2513-2.8367]) and the average outcome differed significantly from zero ($z = 2.3409$, $p = 0.0192$). The Q-test for heterogeneity was not significant, but some heterogeneity may still be present in the true outcomes ($Q[2] = 5.7269$, $p = 0.0571$, $tau^2 = 0.8304$, $I^2 = 66.6143\%$). The 95% prediction interval for the true outcomes was [-0.6608-3.7487]; therefore, although the average outcome is estimated to be positive, in some studies the true outcome may not. None of the studies had studentized residuals larger than ± 2.3940, indicating the absence of outliers in this model. According to the Cook's distances, none of the studies could be considered overly influential. The rank correlation test did not indicate funnel plot asimmetry ($p = 0.3333$). Figure 3 shows the forest plot summarizing these findings, after exponential

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transformation to obtain odds ratios for clearer understanding of the effect size.

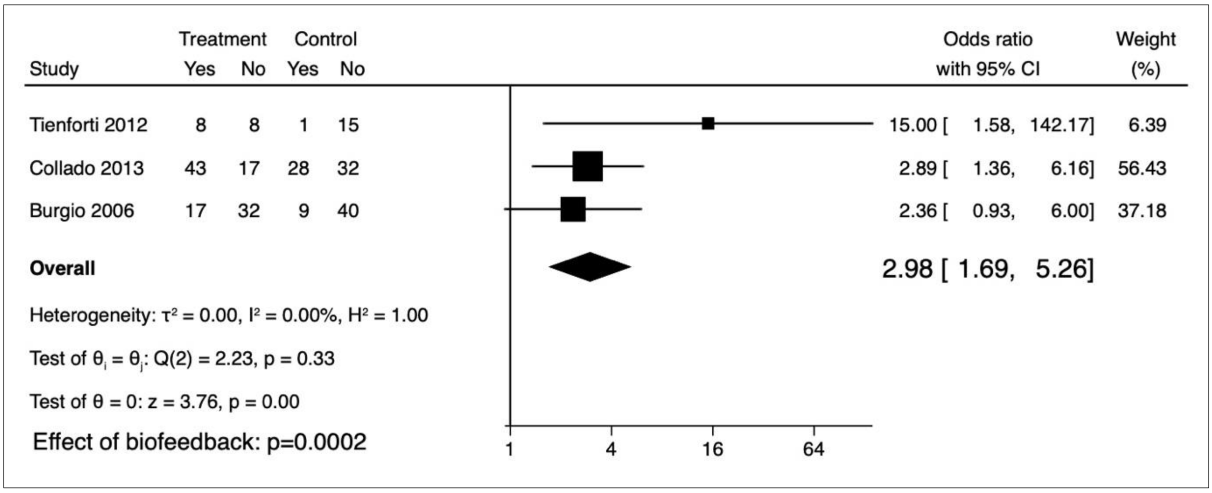

Figure 2: Continence recovery 3 months after surgery

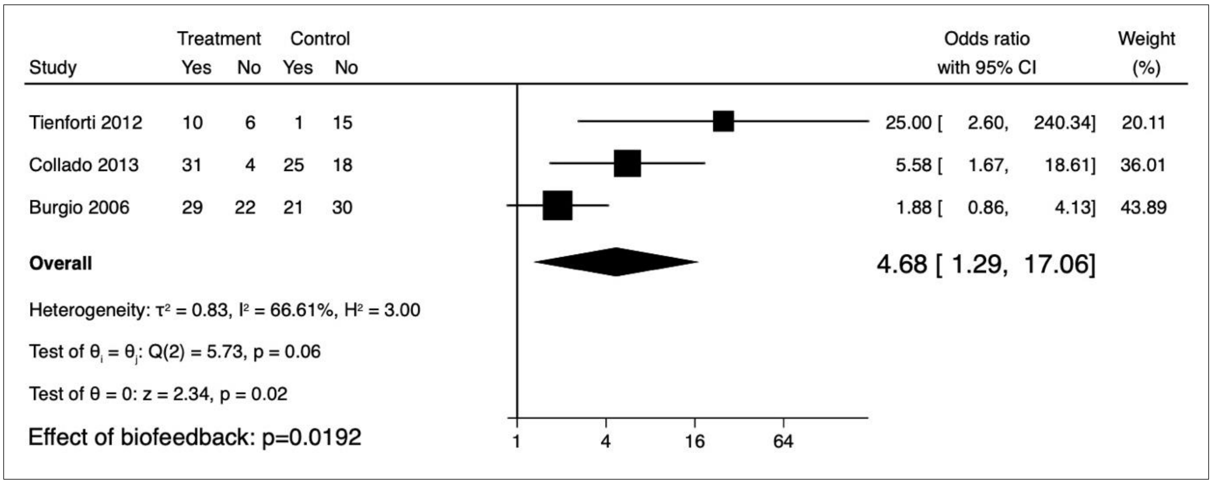

Figure 3: Continence recovery 6 months after surgery

DISCUSSION

Regarding implications for practice, since BFB cannot be separated from PFMT it is necessary to establish precise criteria for preoperative exercises to be performed during BFB. Recommendation for practice can be cautiously based on the studies by Burgio et al. (2006) and Collado et al. (2013), which had the largest effect size in our meta-analysis among those favorable to BFB (figure 2) and provided indications on the timing and criteria of prehabilitation. The authors suggested a complete set of progressively more demanding exercises, for a total of 45 different tasks. These indication complies with the physiology of muscular training, and agrees with studies by other authors [34] regarding pelvic floor muscle training. The only suggestion that should be discouraged regards stopping urine flow as suggested by Burgio et al., since it increases the post-void residual volume and translates into less efficient micturition as highlighted by recent literature [35].

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Some authors [12] recommended patient relaxation during pelvic contraction, which is paramount for muscular performance, as suggested by the literature [36] to avoid apnoea during training and subsequent increase in IAB. Dijkstra-Eshuis and colleagues [24] included the Valsalva manouvre in their preoperative program, but in our opinion this cannot become a universal recommendation: aged patients, such as many of those undergoing prostatectomy, often have cardiologic comorbidities, and therefore any manouvre increasing blood pressure or potentially provoking vagal stimulation should be performed very cautiously. Finally, biofeedback is a widely used method for teaching pelvic floor muscle exercises; however, it requires that patients accept to regularly visit the outpatients, and to use rectal probes. Learning correct muscular contraction is the key to success for any pelvic training program; it is up to healthcare professionals to assess whether patients need BFB or can lear the required exercises without the discomfort caused by such technique. In conclusion, preoperative biofeedback is useful for improving continence at 6 months after surgery.

The main limitation of this paper, apart from the very limited number of eligible articles in the literature, is the degree of completeness of the information found in the retrieved articles, which was highly variable. Most studies (not only those included in the metanalysis) enrolled very small samples and did not specify the statistical power reached by calculations. The papers presented several different BFB protocols, similarly to what happened in the meta-analysis by Chang and colleagues [8]. Few papers provided information on body position during the exercises taught by using BFB, which deeply affects intra-abdominal pressure (IAB) [31]. None provided full details on respiratory pattern assessment, which also affects IAB [32,33]. Some details about the characteristics of the biofeedback programs are lacking, such as presence and shape of obstacles in the visual programme generated by the computer.

CONCLUSION

Preoperative biofeedback is an effective technique to foster continence recovery in patients undergoing open radical prostatectomy after 3 and 6 months from surgery, compared to instructions regarding PFMT. This type of prehabilitation can be managed by several categories of healthcare professionals (i.e., nurse, physiotherapists) in many countries worldwide; therefore, this information will be useful to implement evidence-base programs based on biofeedback.

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Submission received: 23/06/2023
End of Peer Review process: 28/07/2023
Accepted: 30/07/2023

Milano University Press

ISSN: 2785-7263 DOI: 10.54103/dn/20383
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Via Ovada 26, 20142 Milano, Italy
Submission received: 23/06/2023
End of Peer Review process: 28/07/2023
Accepted: 30/07/2023
Milano University Press

ISSN: 2785-7263 DOI: 10.54103/dn/20383

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Accepted: 30/07/2023

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