

FR 322: Psycho-physical prediction of persistent pain after breast cancer surgery ?

Lack of recovery from central sensitization and impaired conditioned pain modulation in patients developing persistent pain after breast cancer surgery

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The study is dedicated to Roberto S.G.M. Perez, an inspiring scientist, mentor and friend

Persistent Pain after Breast Cancer Treatment (PPBCT) affects 25-60% [1] of breast cancer survivors. Comprehensively identifying individual risk factors, including psycho-social and psycho-physical traits is an important step towards personalized prevention strategies. The presented study aimed to test the feasibility of a protocol assessing neurophysiological, psychological, and clinical parameters associated with PPBCT.

Prospective single-center cohort of adult female patients undergoing unilateral surgery for breast cancer. Primary objective was the incidence of PPBCT one year after surgery.

Psycho-social and clinical parameters, as well as somatosensory sensitivity were assessed at baseline (preoperative), and at 10 days, 4 and 12 months with a short form of the DFNS QST protocol [2] combined with the NASQ protocol [3].

Conditioned pain modulation (CPM) was assessed with a pressure pain-cold pressor algorithm [4].

Parameter	no PPBCT n=9	PPBCT n=4	P
Age [years]	57.22	52.5	0.162
BMI [kg/m ²]	26.4	30.7	0.058
Tumor classification [TNM]			
T1N0	2	1	
T1N1	0	0	
T1N0M0	5	2	
T1N1M0	2	0	
T2N3M0	0	1	0.367
Type of surgery [n]			
Wide local excision	7	3	
Mastectomy	2	1	
Lymph node handling [n]			
Sentinel node	8	3	
Axillary dissection	0	1	0.252
Radiation therapy [n]	8	3	
Expectation of post-operative pain intensity [NRS]	4.56	7.25	0.008
Preoperative pain in surgical area			
BPI severity	0.75	4.1	0.488
BPI interference	0	2.1	0.408
Preoperative other chronic pain complaints			
BPI severity	3.4	5.5	0.065
BPI interference	1.1	4.1	0.077
Post-operative pain (NRS)			
Day 1	2.6	3.8	0.245
Day 2	2.6	4.4	0.087
Day 3	2.0	3.2	0.100
Concerns about recurrence [CARS]	11.56	9.25	0.351
Quality of life EORTC			
QoL C30	79.6	79.2	
BR 23 Functional	4.6	23.0	0.022
BR 23 symptoms	0	19.5	0.005
Anxiety [STAI]	1.8	1.6	0.307
Pain catastrophizing [PCS]	7.7	9.8	0.642
Dispositional optimism [LOT-R]	21.9	19.5	0.243
Social support [mMOS-SS]	90.6	77.3	0.092
Depression [CES-D]	10.6	14.8	0.188

Table 1: Baseline characteristics of the breast cancer patients with 12 months follow-up & risk factor analyses

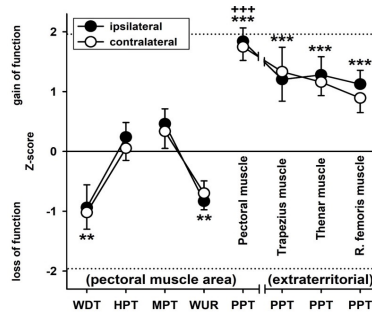


Figure 1: QST profile at baseline assessed in the pectoral area at the site of surgery (black dots) and contralateral mirror image (white dots) and pressure pain thresholds at extrateritorial muscle test sites. **p*<0.01, ***p*<0.01 vs. healthy age matched standard population derived from the DFNS data base [5,6], ****p*<0.01 vs extrateritorial sites

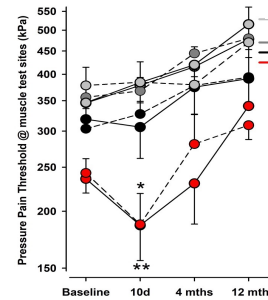


Figure 2: Pressure pain thresholds (PPT) at baseline and follow-up at the pectoral (red dots), trapezius (black dots), thenar (dark grey dots) and rectus femoris muscles (light grey dots), solid lines ipsilateral, broken lines contralateral to the surgical site. Sensitization after surgery vs. baseline **p*<0.05 contralateral, ***p*<0.01 ipsilateral

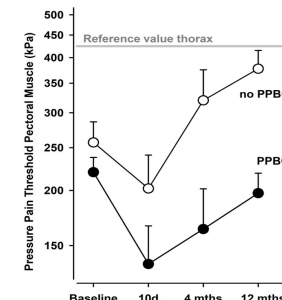


Figure 3: Development of PPT with regards to presence (black dots, n=4) or absence (white dots, n=9) of PPBCT

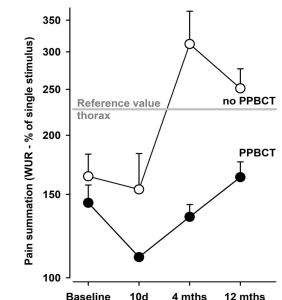


Figure 4: Development of pain summation (WUR) at baseline (preoperative) and during follow-up in patients with PPBCT (black dots, n=4) or without PPBCT (white dots, n=9).

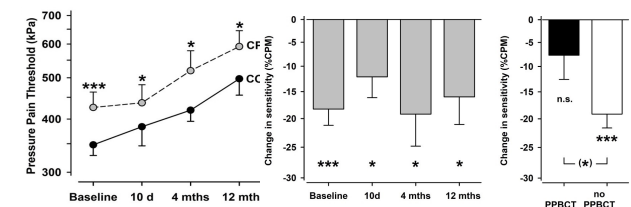


Figure 5: Left panel: Pressure pain thresholds before (black dots) and after CPM (grey dots) Middle & right panel: CPM all patients (grey bars, mean ± SEM), stratified by presence (black bar) or absence (white bar) of PPBCT. **p*<0.05, ****p*<0.001, **p*=0.057 vs. PPT prior to CPT

20 patients gave informed consent, 7 were excluded or lost.

Of the remaining 13, 4 patients (31%) retained PPBCT. Mean PPBCT intensity was NRS 4.25 ± 1.5, maximum intensity NRS 6.5 ± 2.4. PPBCT patients had a higher BMI, more preoperative pain in the surgical area and elsewhere, more intense expected and experienced postoperative pain, together with a lower quality of life, less social support, more depression and less optimism (n.s.) (Tab.1).

QST at preoperative baseline revealed bilateral hypesthesia for warmth, reduced temporal summation of pain and a body-wide generalized hyperalgesia to blunt pressure that was most pronounced at the pectoral muscle, while heat (HPT) and pricking pain threshold (MPT) were unchanged (Fig.1). During follow-up, after a transient postoperative further drop in pressure pain thresholds, PPTs (Fig.2) and WURs returned to healthy control values. Stratification revealed that normalization occurred on in patients without PPBCT, while recovery was absent in patients with PPBCT (Figs.3 and 4).

The cold pressor test (CPT) elicited a 17% increase in pressure pain thresholds (CPM) (Fig.5 left/middle). Patients with PPBCT rated CPT pain higher (86 ± 14 vs. 69 ± 20 NRS), withdrew their hands earlier (34 ± 17 vs. 68 ± 62 seconds) and - in contrast to patients without PPBCT - exhibited no significant CPM (Fig 5 right).

The one-year incidence of PPBCT was 31%. The known risk factors high BMI, preoperative pain in the surgical area, high postoperative pain intensity and unfavourable psycho-social profile were confirmed.

QST and CPM point towards a lack of recovery from preceding central sensitization and concomitant reduced descending noxious inhibitory control as underlying mechanisms.

Multifactorial prediction tools for PPBCT should assess central sensitization with QST and CPM before and shortly after surgery in combination with parameters of psycho-social distress, carefully considering patient burden.