

INTRODUCTION

Although prostate cancer (PCa) is now most often detected in its early stages, still a relevant number of patients are found to have locally advanced disease. Recent data from European and US studies provide an estimation of the incidence of cT3-4 PCa, which is thought to be 10-20%. The optimal treatment for cT3 PCa has been subject to debate during recent years. According to EAU guidelines on treatment of PCa radical prostatectomy in locally advanced disease is an option for selected patients with small unilateral T3 cancers, PSA lower than 20 ng/mL, a Gleason score lower than 8 and a life expectancy of more than 10 years.

To evaluate our results in this matter we have conducted a retrospective study in 240 patients who underwent an endoscopic extraperitoneal radical prostatectomy (EERPE) at our non-academic center in the Netherlands. We further investigated the results of 78 patients with pT3-4 PCa to better define the place of surgery in locally advanced disease.

PATIENTS AND METHODS

From May 2006 to February 2012 we performed 240 EERPE's in men with PCa. Based on guidelines and nomograms a laparoscopic lymph node dissection (LPLND) was performed in 164 cases (69%) using the current standard template. All procedures were performed by the same surgeon. Information regarding operating time, blood loss, hospital stay, catheterization time, pathological data and functional outcome were collected prospectively in our patient database. We retrospectively analyzed the charts of 78 patients (32,5%) with confirmed locally advanced disease for further information on preoperative staging, complications and mid-term oncological follow-up. For biochemical progression-free survival estimates we used Kaplan-Meier curves of SPSS 20.0. For statistical analysis we used the chi-square- and log rank test. PSA recurrence was defined as a rise of PSA above 0,2 ng/mL in at least 2 consecutive laboratory tests.

Patient characteristics	Localized PCA (≤pT2c, n=162)	Locally advanced PCA (pT3-4, n=78)
Age (years), mean (±SD)	63,8 (5,9)	65,5 (5,7)
PSA (ng/mL), mean (range)	10,9 (0,87-71)	18,3 (2,1-190)
Prostate volume (mL), mean (range)	40,1 (10-136)	38,1 (10-82)
Hospital stay (days), mean	5,4	5,3
Catheterization time (days), mean	16	18
Perioperative data		
Estimated blood loss (mL), median	400	500
Operating time (minutes), median	219	218
EERPE	171	169
EERPE+LPLND	250	225
Nerve sparing procedure, n (%)	84 (51,2%)	15 (19,4%)
Lymphadenectomy not performed, n (%)	61 (37,4%)	14 (18,4%)
Lymphadenectomy in 2 stages, n (%)	3 (1,8%)	7 (9,1%)
Pathology		
Biopsy Gleason score, mean (range)	6,1 (4-9)	6,6 (5-10)
Pathological Gleason score, mean (range)	6,4 (4-9)	7,1 (4-9)
Lymph nodes removed, n (range)	12,5 (1-56)	12,3 (2-29)
LNI, n (%)	2 (1,2%)	13 (16,8%)
Positive surgical margins, n (%)	37 (22,8%)	47 (60,3%)

Table 1. Patient characteristics, perioperative- and pathological data. LNI=lymph node invasion. Bold characters means a statistically significant difference (p<0,05).

Positive surgical margins	n (%)
All patients	85 (35,4%)
pT2	37 (22,8%)
pT3a	23 (51,1%)
pT3b	22 (68,8%)
pT4	1 (100%)

Table 2. Comparison between positive surgical margins and pathological stage after laparoscopic prostatectomy

	pT2	pT3-4	
cT2	154	52 (25,2%)	206
cT3-4	8 (23,5%)	26	34
	162	78	240

Table 3. Clinical over- and understaging. Staging based on digital rectal examination, ultrasound and occasionally MRI.

	pN1	pN0	
rN1	1	5	6
rN0	9	28	37
	10	33	43

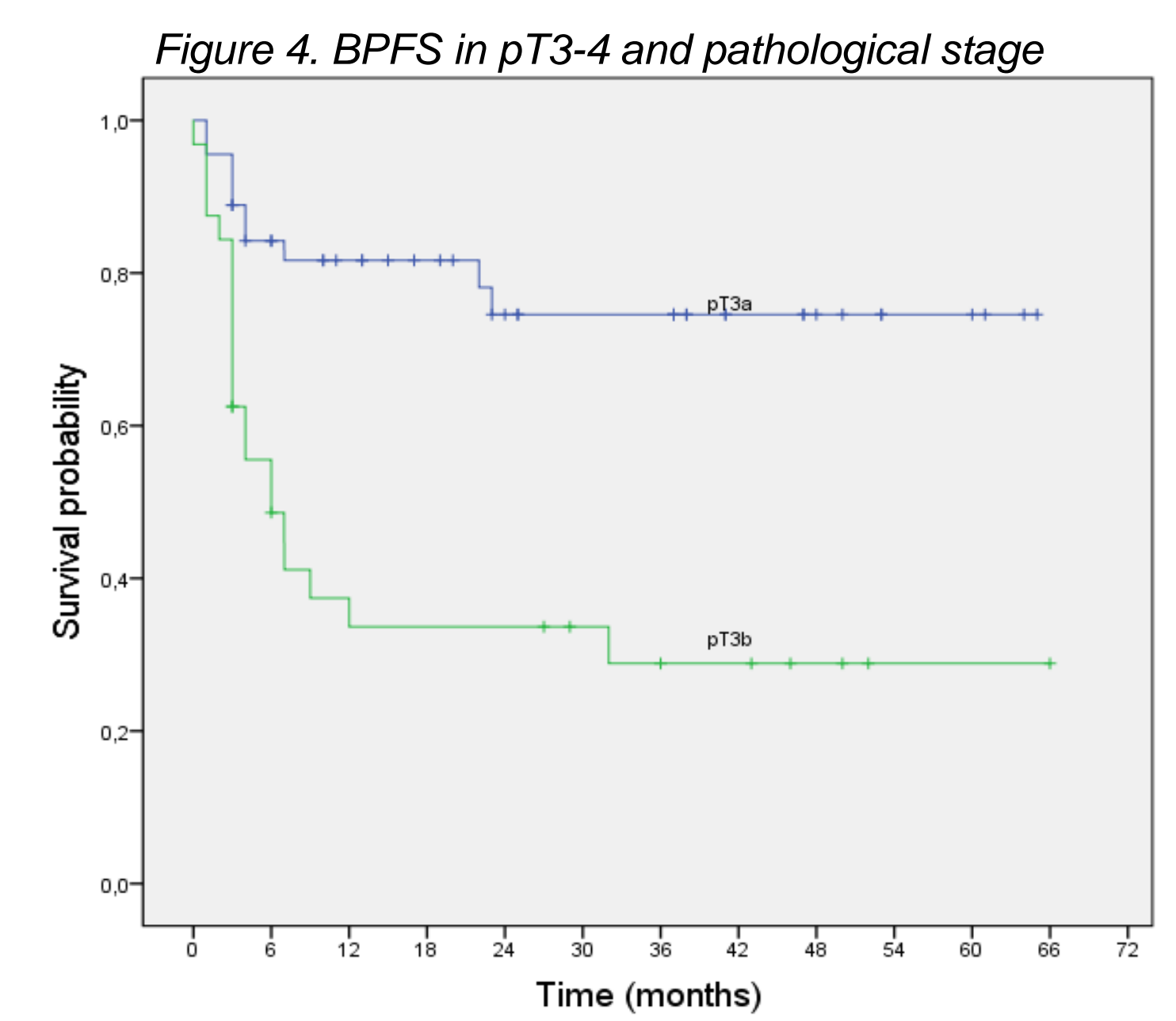
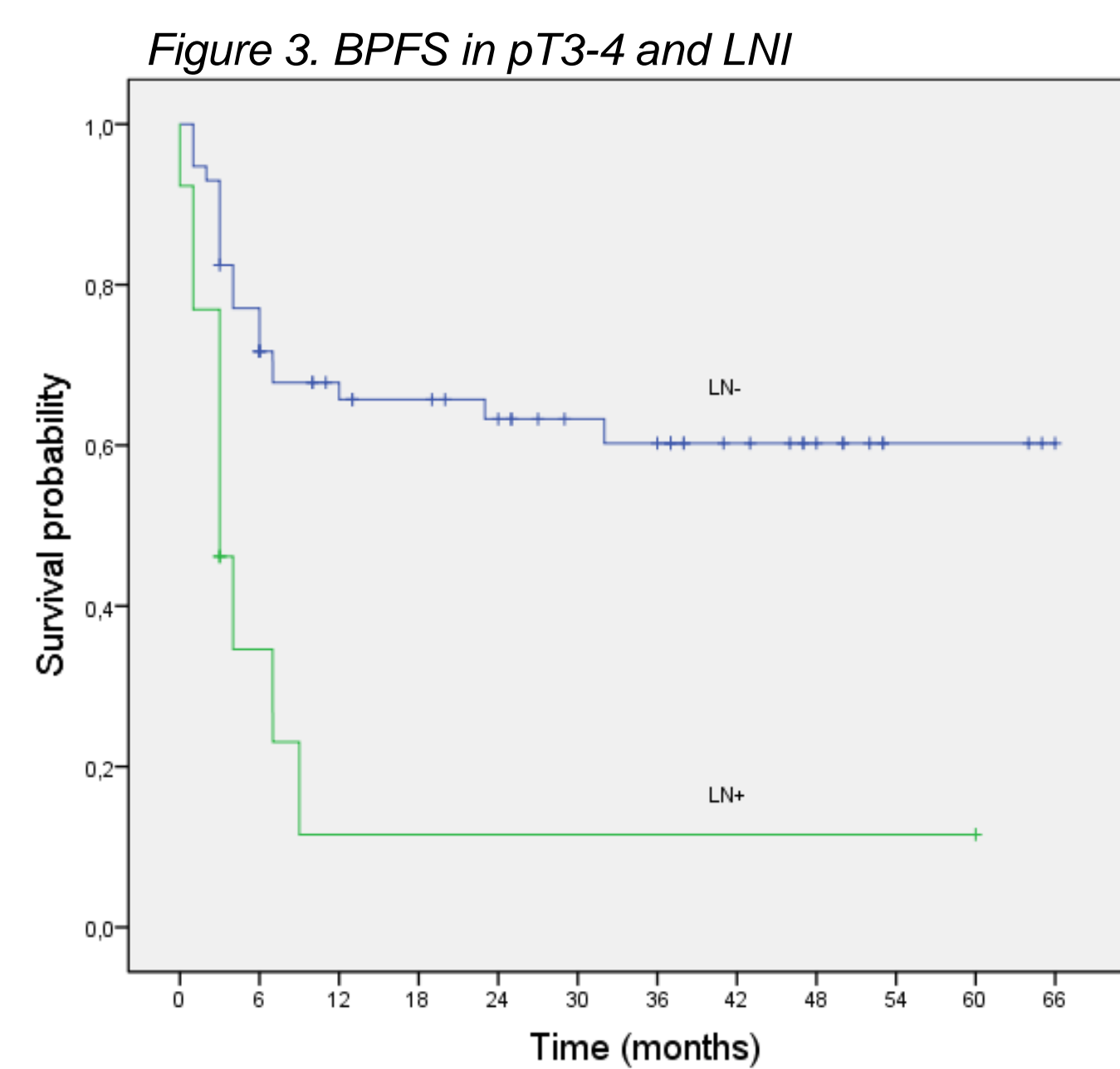
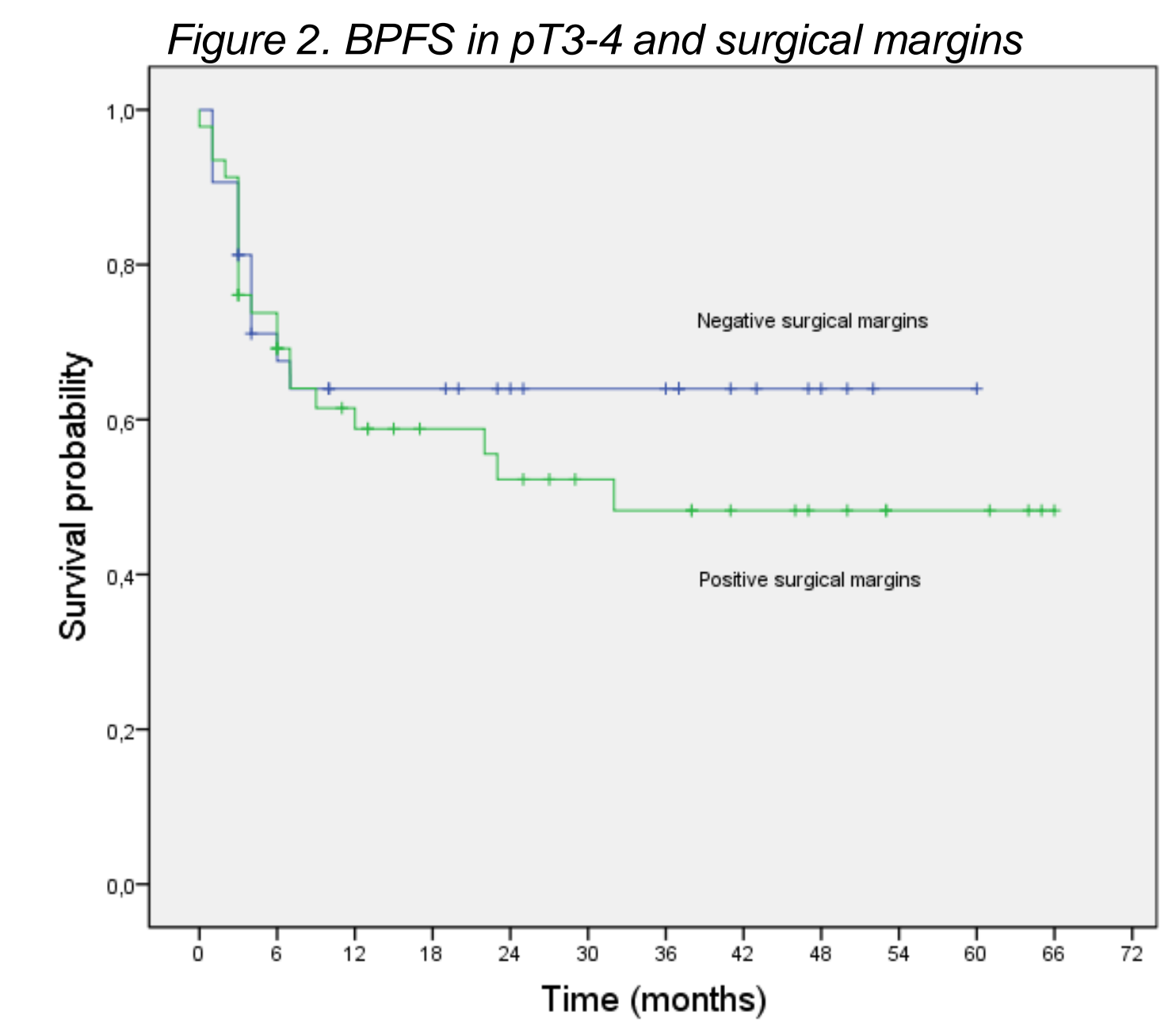
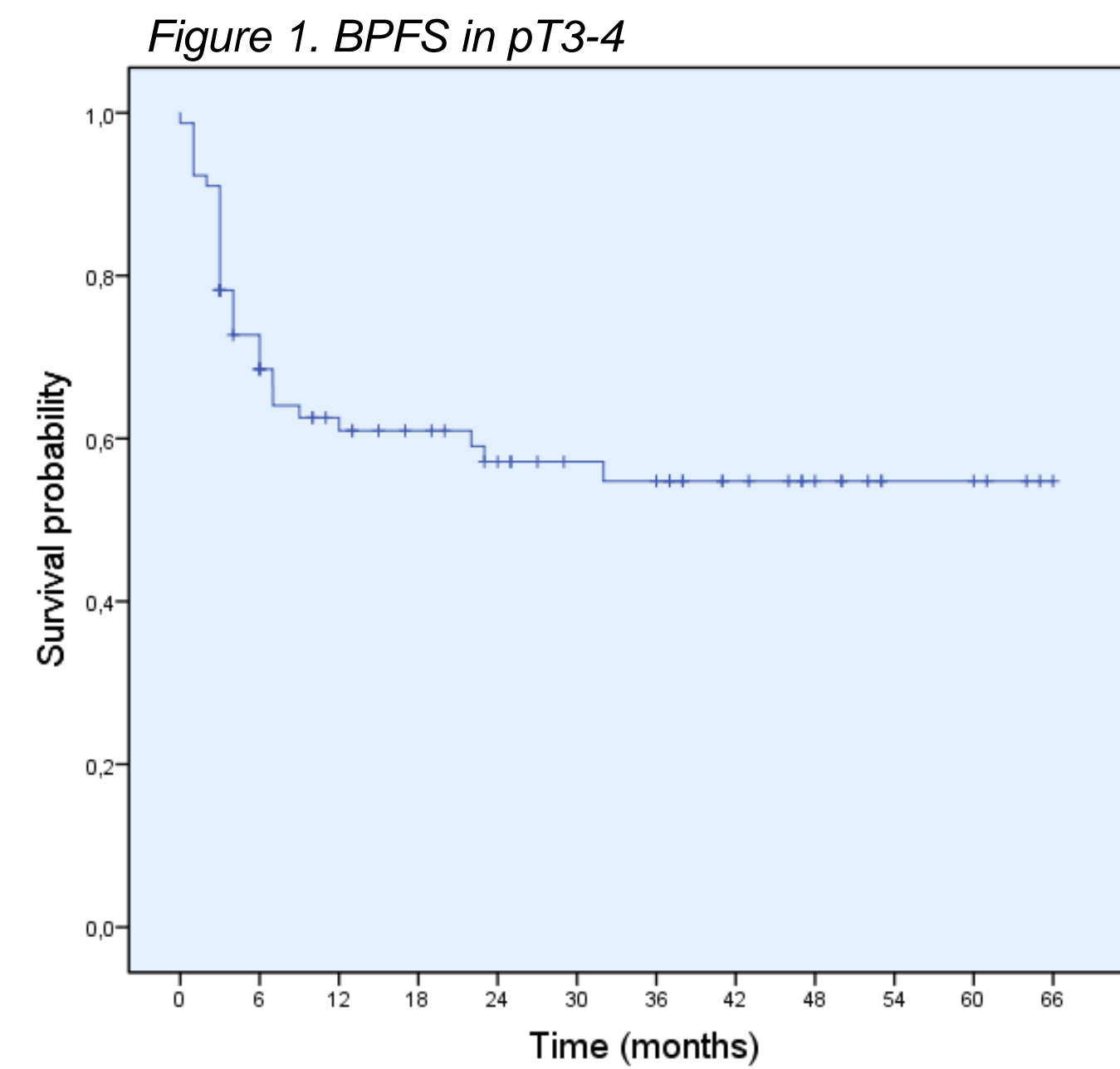
Table 4. Value of MRI in predicting LNI. Sensitivity 0,10, specificity 0,90, PPV 0,17, NPV 0,76. LNI=lymph node invasion, PPV=positive predictive value, NPV=negative predictive value

Postoperative complications	n
I	7
II	10
IIIa	12
IIIb	4
IV	0
V	0

Table 5. Postoperative complications according to the Clavien-Dindo classification.

CONCLUSION

In our study locally advanced PCa's have a higher iPSA-level, pathological Gleason score, higher risk of lymph node invasion and positive surgical margins. Preoperative staging remains difficult, even with the use of MRI. Oncological results are promising especially for pT3a PCa without lymph node invasion. Therefore efforts have to be made for better patient selection. In case of positive surgical margins and rising PSA, salvage EBRT/IMRT seems beneficial.



RESULTS

Patient characteristics, perioperative- and pathological data are shown in table 1. In the locally advanced group 45 patients were staged as pT3a (18,8%), 32 pT3b (13,3%) and 1 pT4 (0,4%). In table 2 we highlight the comparison between surgical margins and pathological stage. Table 3 shows clinical over- and understaging in 23,5% and 25,2% respectively. In the locally advanced group, 43 preoperative MRI's were made in an attempt to stage PCa more accurately. With the use of this modality there still was understaging in 26 of 43 patients (60,5%). Prediction of lymph node invasion (LNI) with MRI also seems difficult (table 4). Thirty-three postoperative complications occurred in 30 patients (table 5) including 4 colostomies because of rectal injury and subsequent sepsis or fistula (Clavien 3b). No perioperative mortality was noted. Mean follow up of the study was 30,5 months (range 3-61). During this period of time 2 patients died, 1 as a result of PCa (CSS 97,5%). Three year biochemical progression-free survival (BPFS) was 55%. Subgroup analysis showed a significant difference in BPFS between LN+/LN- and pT3a/pT3b (p<0,05). No significance was reached for surgical margins (figures 1-4).