Guidelines recommend an extended pelvic lymph node dissection (ePLND) along with the radical prostatectomy (RP) if the estimated risk of lymph node (LN) metastases exceeds 5% [1]. Besides more accurate staging, the potential survival benefit of the LND is yet to be proven [2,3]. While women operated for cervical cancer with a similar ePLND template have a patient-reported occurrence of lymphoedema of ~35% [4], the staff-reported frequency of lymphoedema after RP ranges from 0% to 10% [5,6], and there is a need for better understanding of the trade-off between benefits and costs of the LND in prostate cancer.

We assessed the risk of groin and leg swelling after RP using patient-reported data within the prospective Laparoscopic Prostatectomy Robot Open (LAPPRO) trial [7]. We evaluated the effect of the extent of the LND, the surgical approach, and the surgeons’ experience on the risk of groin and leg swelling, and to what extent any swelling impacts the quality of life.

The prospective controlled trial LAPPRO is a non-randomised multicentre trial including patients treated at 14 Swedish urological centers. We included patients aged <75 years who were operated for localised prostate cancer between 1 September 2008 and 7 November 2011. An ePLND was done according to the local criteria at the participating centers. The design and data collection of the LAPPRO trial have been described in detail previously [7].

The study patients completed validated questionnaires at 3, 12 and 24 months after surgery. We assessed the prevalence of patient-reported groin and leg swelling using the following questions at 3 months postoperatively: ‘Have you had swelling in the left/right groin after surgery?’, and ‘Have you had swelling in the left/right leg after surgery?’. Patient-reported quality of life was evaluated using the following questions: ‘How would you like to describe your quality of life in the past month?’ and ‘How do you rate your physical health in the past month?’. Staff-reported occurrence of swelling was assessed using the following questions recorded at 3, 12, and 24 months after surgery: ‘Is there a swelling (sign of lymphoedema) in the groins?’ and ‘Is there a swelling (sign of lymphoedema) in the legs?’. We also used perioperative case report form (CRF) data to ascertain the following information: robot-assisted laparoscopic RP (RALP) or open surgical approach (retropubic RP [RRP]), extent of LND, and surgeons’ experience. Data on LN yield was extracted from the pathology report.

We estimated crude and adjusted risks for different outcomes with multinomial logistic regression. The independent variables, all categorical, entered the regression models by means of indicator variables. The association of the outcome variables with the independent variables was summarised by relative risk ratios (RRs) with 95% CIs. We set the level of all our statistical tests at 5%. The analyses were performed with Stata statistical software, version 15 (StataCorp, College Station, TX, USA).

Out of 3675 men in the study, LND was done in 645 (17.6%; Table 1). At 3 months after RP, the prevalence of patient-reported moderate-to-severe swelling of the groin and leg was 13.7% (95% CI 11.1%–16.6%) among men who had undergone LND, compared with 3.0% (95% CI 2.5%–3.8%) among men who had not (Table 1). The staff-reported (CRF) prevalence of swellings was lower than the patient-reported, but repeated measurements over time indicates stable prevalence from 3 to 24 months after surgery.

The adjusted RR for the association between LND and moderate-to-severe swelling in the groin and legs at 3 months was 6.9 (95% CI 4.7–10.1; Table 2). Low surgical experience was not associated with reported swelling of the groin and leg, nor was there any clear difference between RALP and RRP (Table 2).

After adjusting for other side-effects, such as erectile dysfunction and incontinence, the adjusted relative risk for worst quality of life and physical health (patient-reported) was significantly increased among men with swelling of the groin or leg, or reported signs of swelling of groin and leg. This negative effect seemed to remain at 12 months after surgery, but decreased and was not statistically significant at 24 months postoperatively (Table 3).

We found a fourfold increased prevalence of patient-reported swelling in the groin and leg associated with the LND. Swelling symptoms remained at 12 and 24 months after surgery, and seemed to profoundly affect perceived physical health and quality of life. While staff-reported frequency of groin and leg swelling was 5%, 14% of our patients reported swellings at 3 months after surgery. Previous studies’ findings of between 0% and 10% prevalence of swellings based on staff reports may likely have been underestimations.

We also found that swellings of the groin and leg negatively affect the patients’ quality of life and physical health. Swelling after LND has been carefully studied and recognised in breast
Table 1 Postoperative lymph swelling after RP in relation to LND, surgical experience, and surgical technique.

| Swelling of grain or leg at 3 months after RP | Patient-reported | Doctor-reported |
|-----------------------------------------------|------------------|------------------|
|                                               | N (%) | Adj RRa | P     | N (%) | Adj RRb | P     |
| LND                                            |       | Adj RRb | P     |       | Adj RRb | P     |
| Yes                                           | 437 (70.4) | 3.1 (2.3-4.1) | <0.001 | 69.8 (4.7-10.0) | 3.1 (2.3-4.1) | <0.001 |
| No                                            | 2578 (88.8) | 1.6 (0.9-2.7) | 0.075 | 1.2 (0.7-2.1) | 0.44 |
| LN yield                                      |       |        |       |       | Adj RRb | P     |
| 1-4                                          | 47 (79.7) | 1.0 (0.4-2.3) | 1.0 (0.4-2.3) | 1.0 (0.4-2.3) | 1.0 (0.4-2.3) | 1.0 (0.4-2.3) |
| 5-9                                          | 70 (68.6) | 0.8 (0.2-2.2) | 0.63 | 3.8 (0.7-19.8) | 0.096 |
| 10-19                                        | 93 (62.8) | 0.9 (0.3-3.5) | 0.84 | 5.7 (1.2-26.5) | 0.025 |
| ≥20                                          | 94 (69.1) | 1.0 (0.9-2.5) | 0.98 | 2.9 (0.61-14.3) | 0.178 |
| Surgeon experience                            |       | Adj RRb | P     |       | Adj RRb | P     |
| <50                                          | 398 (87.0) | 3.1 (2.3-4.1) | <0.001 | 69.8 (4.7-10.0) | 3.1 (2.3-4.1) | <0.001 |
| <100                                         | 417 (87.8) | 1.6 (0.9-2.7) | 0.075 | 1.2 (0.7-2.1) | 0.44 |
| <200                                         | 790 (84.3) | 0.8 (0.2-2.2) | 0.63 | 3.8 (0.7-19.8) | 0.096 |
| ≥200                                         | 1396 (85.1) | 0.9 (0.3-3.5) | 0.84 | 5.7 (1.2-26.5) | 0.025 |
| RALP                                          | 729 (80.7) | 1.0 (0.9-2.5) | 0.98 | 2.9 (0.61-14.3) | 0.178 |
| RALP vs RRPb                                  | 2309 (87.1) | 1.2 (0.60-2.51) | 0.57 | 0.9 (0.44-1.87) | 0.79 |

Abbreviations: RALP, robot-assisted laparoscopic RP; RRP, retropubic RP. As defined at operation by surgeon. As described in pathology report.

Table 2 Risk factors for lymph swelling after RP.

| Patient-reported | Doctor-reported |
|------------------|------------------|
|                  | 6-12 weeks | 12 months | 24 months |
|                  | Adj RRb | (95% CI) | P       | Adj RRb | (95% CI) | P       | Adj RRb | (95% CI) | P       |
| LND Yes vs no    | 3.1 (2.3-4.1) | <0.001 | 69.8 (4.7-10.0) | <0.001 | 14.1 (6.5-30.5) | <0.001 | 2.7 (1.2-6.3) | 0.014 |
| Ext. vs lim. LN yield | 1.6 (0.9-2.7) | 0.075 | 1.2 (0.7-2.1) | 0.44 | 2.2 (0.9-5.5) | 0.094 | 3.5 (0.9-13.3) | 0.04 |
| Surgical experience | 1.3 (0.9-1.8) | 0.35 | 1.4 (0.7-2.7) | 0.28 | 0.9 (0.3-2.3) | 0.82 |
| Adj RRb | (95% CI) | P       | Adj RRb | (95% CI) | P       | Adj RRb | (95% CI) | P       |
| RALP vs RRPb      | 0.7 (0.3-1.5) | 0.34 | 0.7 (0.3-1.4) | 0.28 | 0.9 (0.4-2.3) | 0.86 |

Abbreviations: Adj., adjusted; Est., extensive; lim., limited. No swelling group was reference category, and was omitted. Adjusted for diabetes, smoking, re-operation, complications, hemia, body mass index, and age. In addition adjusted for LN yield.

cancer [8] and gynaecological cancers, but the condition has received less attention in the context of prostate cancer, despite the fact that the template of the LND is similar to that of several gynaecological cancers. We recommend future studies to confirm our findings using patient-reported measures.

We could not find any correlation between the number of LNs removed and swelling of the groin and leg. However, we found that removal of only one to four LNs compared with ≥10 was associated with a statistically significant difference in swelling. The risk of swelling in the groin/legs was non-significantly increased after extended LND compared with limited LND, but the variation in reported number of LNs from different pathologists may have attenuated this comparison.

The LAPPRO trial is one of the largest and most valid population-based comparisons of RALP and open RRP.
Our use of patient-reported symptoms is a clear strength in this present analysis. Apart from the non-randomised design, the main limitation of the study is that the patient-reported questions on swelling at 3 months were not repeated in subsequent follow-up questionnaires at 12 and 24 months.

In summary, LND during RP was associated with an elevated risk of persisting lymph swelling postoperatively and impacted negatively the quality of life of the patients. These findings suggest that patients should be explicitly informed about lymph swelling as a potentially persisting side-effect. The frequent occurrence of lymph swelling emphasises the need for careful consideration of risks vs potential benefits, and the need for randomised studies evaluating whether or not surgical removal of the LNs entails any important benefit beyond disease staging.

Our use of patient-reported symptoms is a clear strength in this present analysis. Apart from the non-randomised design, the main limitation of the study is that the patient-reported questions on swelling at 3 months were not repeated in subsequent follow-up questionnaires at 12 and 24 months.

In summary, LND during RP was associated with an elevated risk of persisting lymph swelling postoperatively and impacted negatively the quality of life of the patients. These findings suggest that patients should be explicitly informed about lymph swelling as a potentially persisting side-effect. The frequent occurrence of lymph swelling emphasises the need for careful consideration of risks vs potential benefits, and the need for randomised studies evaluating whether or not surgical removal of the LNs entails any important benefit beyond disease staging.

### Conflict of Interest

None declared.

### References

1. Sanda MG, Cadeddu JA, Kirkby E et al. Clinically localized prostate cancer: AUA/ASTRO/SUO Guideline part II: recommended approaches and details of specific care options. J Urol 2018; 199: 990–7.
2. Berglund RK, Sadetsky N, DuChane J, Carroll PR, Klein EA. Limited pelvic lymph node dissection at the time of radical prostatectomy does not

### Table 3

|                        | Patient-reported | Doctor-reported |
|------------------------|------------------|-----------------|
|                        | No, n (%)        | Yes, n (%)      | RR   | P      | RRa (95% CI) | P     |
| **Quality of life**    |                  |                 |      |        |              |       |
| 3 months               |                  |                 |      |        |              |       |
| Good                   | 1426 (47.2)      | 128 (38.0)      | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 1392 (46.0)      | 177 (52.5)      | 1.3  | <0.001 | 1.4 (1.2–1.6) | <0.001 |
| Worse                  | 207 (6.8)        | 32 (9.5)        | 1.5  | <0.001 | 1.6 (1.2–2.0) | <0.001 |
| Physical health        |                  |                 |      |        |              |       |
| Good                   | 1678 (55.4)      | 152 (45.1)      | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 1217 (40.1)      | 158 (46.9)      | 1.5  | <0.001 | 1.6 (1.3–1.8) | <0.001 |
| Worse                  | 135 (4.5)        | 27 (8.2)        | 2.3  | <0.001 | 2.2 (1.7–2.9) | <0.001 |
| **Physical health**    |                  |                 |      |        |              |       |
| Good                   | 1248 (57.8)      | 14 (37.8)       | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 821 (38.0)       | 18 (48.7)       | 1.9  | 0.062  | 1.6 (0.7–3.4) | 0.23  |
| Worse                  | 92 (4.2)         | 5 (13.5)        | 4.8  | 0.003  | 5.7 (1.9–16.4) | 0.002 |
| **12 months**          |                  |                 |      |        |              |       |
| Good                   | 1275 (58.1)      | 12 (31.6)       | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 817 (37.7)       | 24 (63.2)       | 3.1  | 0.001  | 2.9 (1.4–6.0) | 0.006 |
| Worse                  | 76 (3.5)         | 2 (5.3)         | 2.7  | 0.18   | 3.3 (0.7–14.7) | 0.15  |
| **24 months**          |                  |                 |      |        |              |       |
| Good                   | 925 (54.4)       | 20 (48.6)       | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 680 (42.0)       | 16 (45.7)       | 1.4  | 0.33   | 1.4 (0.7–2.9) | 0.37  |
| Worse                  | 59 (3.6)         | 2 (5.7)         | 1.5  | 0.59   | 0.8 (0.1–6.1) | 0.83  |
| **Quality of life**    |                  |                 |      |        |              |       |
| 3 months               |                  |                 |      |        |              |       |
| Good                   | 1426 (47.2)      | 128 (38.0)      | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 1392 (46.0)      | 177 (52.5)      | 1.3  | <0.001 | 1.4 (1.2–1.6) | <0.001 |
| Worse                  | 207 (6.8)        | 32 (9.5)        | 1.5  | <0.001 | 1.6 (1.2–2.0) | <0.001 |
| Physical health        |                  |                 |      |        |              |       |
| Good                   | 1678 (55.4)      | 152 (45.1)      | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 1217 (40.1)      | 158 (46.9)      | 1.5  | <0.001 | 1.6 (1.3–1.8) | <0.001 |
| Worse                  | 135 (4.5)        | 27 (8.2)        | 2.3  | <0.001 | 2.2 (1.7–2.9) | <0.001 |
| **Physical health**    |                  |                 |      |        |              |       |
| Good                   | 1248 (57.8)      | 14 (37.8)       | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 821 (38.0)       | 18 (48.7)       | 1.9  | 0.062  | 1.6 (0.7–3.4) | 0.23  |
| Worse                  | 92 (4.2)         | 5 (13.5)        | 4.8  | 0.003  | 5.7 (1.9–16.4) | 0.002 |
| **12 months**          |                  |                 |      |        |              |       |
| Good                   | 1275 (58.1)      | 12 (31.6)       | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 817 (37.7)       | 24 (63.2)       | 3.1  | 0.001  | 2.9 (1.4–6.0) | 0.006 |
| Worse                  | 76 (3.5)         | 2 (5.3)         | 2.7  | 0.18   | 3.3 (0.7–14.7) | 0.15  |
| **24 months**          |                  |                 |      |        |              |       |
| Good                   | 925 (54.4)       | 20 (48.6)       | 1 (ref) | 1 (ref) |              |       |
| Medium                 | 680 (42.0)       | 16 (45.7)       | 1.4  | 0.33   | 1.4 (0.7–2.9) | 0.37  |
| Worse                  | 59 (3.6)         | 2 (5.7)         | 1.5  | 0.59   | 0.8 (0.1–6.1) | 0.83  |

*Adjusted for age, body mass index, erectile dysfunction, and incontinence.*
affect 5-year failure rates for low, intermediate and high risk prostate cancer: results from CaPSURE. J Urol 2007; 177: 526–30.

3 Murphy AM, Berkman DS, Desai M, Benson MC, McKiernan JM, Badani KK. The number of negative pelvic lymph nodes removed does not affect the risk of biochemical failure after radical prostatectomy. BJU Int 2010; 105: 176–9

4 Carlson JW, Kauderer J, Hutson A et al. GOG 244 – the lymphedema and gynecologic cancer (LEG) study: incidence and risk factors in newly diagnosed patients. Gynecol Oncol. 2020; 156: 467–74

5 Stone NN, Stock RG, Unger P. Laparoscopic pelvic lymph node dissection for prostate cancer: comparison of the extended and modified techniques. J Urol 1997; 158: 1891–4.

6 Clark T, Parekh DJ, Cookson MJ et al. Randomized prospective evaluation of extended versus limited lymph node dissection in patients with clinically localized prostate cancer. J Urol 2003; 169: 145–8.

7 Thorsteinsdottir T, Stranne J, Carlsson S et al. LAPPRO: a prospective multicentre comparative study of robot-assisted laparoscopic and retropubic radical prostatectomy for prostate cancer. Scand J Urol Nephrol 2011; 45: 102–12.

8 Ahmed RL, Prizment A, Lazovich D, Schmitz KH, Folsom AR. Lymphedema and quality of life in breast cancer survivors: the Iowa Women’s Health Study. J Clin Oncol 2008; 26: 5689–96.

Correspondence: Stefan Carlsson, Department of Molecular Medicine and Surgery, Section of Urology, Karolinska Institute, Stockholm, Sweden.

e-mail: stefan.carlsson@ki.se

Abbreviations: CRF, case report form; (e)(P)LND, (extended) (pelvic) lymph node dissection; LAPPRO, Laparoscopic Prostatectomy Robot Open; LN, lymph node; RALP, robot-assisted laparoscopic RP; (R)RP, (retropubic) radical prostatectomy; RR, risk ratio.