

## Original Article



# Development of the short version of the Gynecologic Cancer Lymphedema Questionnaire: GCLQ-7

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## ABSTRACT

**Objective:** The Gynecologic Cancer Lymphedema Questionnaire (GCLQ) was designed to identify gynecologic cancer patients with lower limb lymphedema (LLL). The questionnaire consists of 20 items distributed over 7 symptom clusters. The present study aimed to develop an abridged form of the GCLQ for simpler screening and more effective follow-up of LLL.

**Methods:** Data that had been collected for the development and validation of the Korean version of the GCLQ (GCLQ-K) were used in this study. Receiver-operating characteristic (ROC) curves were drawn according to the individual items of the GCLQ-K. Based on discrimination ability, the candidate items were selected in each symptom cluster. After combining the items, the best model was identified and named GCLQ-7. The area under the ROC curve (AUC) was compared between the GCLQ-7 and the original GCLQ-K.

**Results:** In total, 11 candidate items were selected from the original GCLQ-K. Among the models made with the candidate items, GCLQ-7, the best model, was constructed with 7 items as follows: 1) limited knee movement, 2) general swelling, 3) redness, 4) firmness/tightness, 5) groin swelling, 6) heaviness, and 7) aching. This model exhibited an AUC of 0.945 (95% confidence interval [CI], 0.900–0.991), which is comparable with that of the original GCLQ-K (AUC, 0.867; 95% CI, 0.779–0.956). The best cutoff value was 2 points, at which the sensitivity and specificity were 97.0% and 76.5%, respectively.

**Conclusion:** The newly developed short version model, GCLQ-7, showed acceptable discrimination ability as compared with the original GCLQ-K.

**Keywords:** Genital Neoplasms, Female; Uterine Cervical Neoplasms; Ovarian Neoplasms; Endometrial Neoplasms; Lymphedema; Surveys and Questionnaires

## INTRODUCTION

In Korea, the annual number of cases of cervical, ovarian, and endometrial cancers is gradually increasing from 6,394 in 1999 to 7,454 in 2010 [1]. In gynecologic cancer surgeries,

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**Conflict of Interest**

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pelvic lymph node dissection (LND) is frequently performed with the purpose of staging and/or reducing tumor burden. However, this procedure causes damage to the lymphatic system, resulting in lower limb lymphedema (LLL) which is one of the most common and bothersome complications for gynecologic cancer survivors [2-5].

To date, the relationship between LLL and quality of life (QOL) in gynecologic cancer survivors has been well investigated. Patients with LLL have annoying lymphedema-related symptoms (e.g., swelling and numbness) and limited leg movement [2-5]. As these conditions deteriorate mobility and daily activity, lymphedema negatively affects cancer survivors' physical, psychological, and social well-being [6,7]. Unfortunately, no cure has yet been established for LLL. Treatment of lymphedema, such as exercise, massage, and compression, focuses on reducing the swelling and controlling the pain. Initiation of treatment as early as possible, before extensive, irreversible changes occur, is recommended [8,9]. Therefore, early detection of LLL is the key point in both prognosis and management.

The Gynecologic Cancer Lymphedema Questionnaire (GCLQ) is a well-studied and useful diagnostic tool that effectively screens gynecologic cancer patients with LLL. This self-reporting questionnaire consists of 20 items that are distributed over 7 clusters of symptoms within the previous 4 weeks, and each item is responded to with either a "no" or a "yes" [10]. GCLQ has been translated into multiple languages. The Korean version of the GCLQ was also developed and validated for the Korean population and termed GCLQ-K [11]. Meanwhile, GCLQ should not be performed as a one-time test among gynecologic cancer survivors. According to a population-based study of Beesley et al. [2], only 75% of LLL cases were diagnosed within the first year after confirmation of gynecologic cancer. Continuous and repetitive follow up tests for LLL are mandatory.

For early detection and effective follow-up tests, a more simplified screening tool is necessary. Thus, the aim of this study was to develop an abridged form of GCLQ. Through statistical analyses, several items would be selected among the existing items of the original GCLQ and these would be used in the construction of possible models.

## MATERIALS AND METHODS

This secondary analysis of our previous retrospective cohort study was conducted after obtaining approval by the Institutional Review Board of National Cancer Center (NCC2016-0059). Data that had been collected for the development and validation of the GCLQ-K were used in this study [11].

### 1. Study population

The study population of the present study was the same as that in our previously published study that developed and validated the GCLQ-K [11]. Among the survivors of gynecologic cancers who visited the outpatient clinic of National Cancer Center between October 2012 and January 2013, the following patients were included: 1) those with older than 18 years, 2) those who underwent pelvic LND, 3) those whose interval from surgery to survey was more than 6 weeks, and 4) those who agreed to participate in the study by providing written informed consent. Meanwhile, the patients with the following conditions were excluded: 1) edema with unclear cause, 2) active thrombosis, 3) tumors or local infection in the lower extremity, 4) uncontrolled diabetes mellitus, 5) severe cardiac dysfunction, 6) renal

insufficiency, 7) auto-immune vasculitis, 8) pregnant or lactating patients, 9) alcohol or drug abusers, and 10) long-term users of systemic corticosteroids.

Of the 67 gynecologic cancer survivors who met these criteria, 33 were identified as having LLL (study group) and the other 34 did not have LLL (control group) [11]. In the diagnosis of LLL, clinicians performed patients' physical examination and limb volume measurement. Imaging modalities such as magnetic resonance imaging or computed tomography (CT), as well as lymphoscintigraphy, were used. To exclude deep vein thrombosis, all the patients with swollen lower extremities were evaluated by using either limb sonography or CT venography, or both [11,12]. All the patients in both groups completed the GCLQ-K survey at the outpatient clinic [11].

## 2. Item selection and model generation

The original GCLQ-K has 20 items distributed over 7 symptom clusters, and each item is responded to with either a "no" or a "yes," scored as 0 or 1, respectively. To develop an abridged form of the GCLQ-K, adequate selection of items was necessary.

First, 20 receiver-operating characteristic (ROC) curves, 1 for each item, were drawn. The performance of the ROC curve was defined as the ability to differentiate patients with LLL from those without LLL. Then, the ROC curves were grouped according to the 7 symptom clusters. The area under the curve (AUC) of the ROC curve was used to identify the most discriminative items. The item with the highest AUC was selected as having the best discrimination performance in each cluster. This procedure would identify 7 items that would be combined to generate a model. However, when the AUCs of the items did not show significant differences within a cluster, 1 or 2 items could be selected in that cluster and generate several different models.

In the comparison of the AUCs among the models, the best model with the best discrimination ability was identified and named GCLQ-7.

## 3. Statistical analysis

The total score for GCLQ-7 was measured by counting the number of items with "yes" responses (range, 0–7). The best cutoff GCLQ-7 score to dichotomize the patients with and without LLL was determined using Youden's index.

The internal consistency reliability of the short version model, GCLQ-7, was assessed by using Cronbach's  $\alpha$  coefficient. The GCLQ-7 was compared with the original GCLQ-K in terms of discrimination ability based on AUCs and their confidence intervals (CIs).

Statistical analysis was performed by using the R statistical software version 2.12.1 (R Foundation for Statistical Computing, Vienna, Austria; ISBN 3-900051-07-0; <http://R-project.org>).

## RESULTS

The patients' clinical characteristics were the same as presented in our previously published study: of the 67 gynecologic cancer survivors, 29, 24, and 12 patients were diagnosed with cervical, ovarian, and endometrial cancer, respectively, and the proportions of each cancer types were not statistically different between the study group and the control group [11].

The ROC curves of the 20 items grouped according to symptom clusters are shown in **Fig. 1**. Under the swelling-general, swelling-limb, heaviness, and aching clusters, “swelling (item 8),” “groin swelling (item 19),” “heaviness (item 14),” and “aching (item 17)” were selected as candidate items for the short version model of GCLQ-K (AUCs, 0.970, 0.743, 0.805, and 0.656, respectively; **Table 1**).

In the physical functioning cluster, the 2 items with the highest AUCs were “leg or foot weakness (item 6)” and “limited knee movement (item 2)” (0.595 and 0.517, respectively), and thus considered as candidate items.

In the infection-related cluster, both “redness (item 10)” and “increased temperature in the leg (item 13)” showed similar AUCs (0.592 and 0.578, respectively), and considered as candidate items.

In the numbness cluster, all 4 items showed similar trends of the ROC curves. Except for “tenderness (item 7),” which showed the lowest AUC (0.577), “firmness/tightness (item 12),” “numbness (item 15),” and “stiffness (item 16)” were all considered as candidate items (AUCs, 0.653, 0.597, and 0.623, respectively).

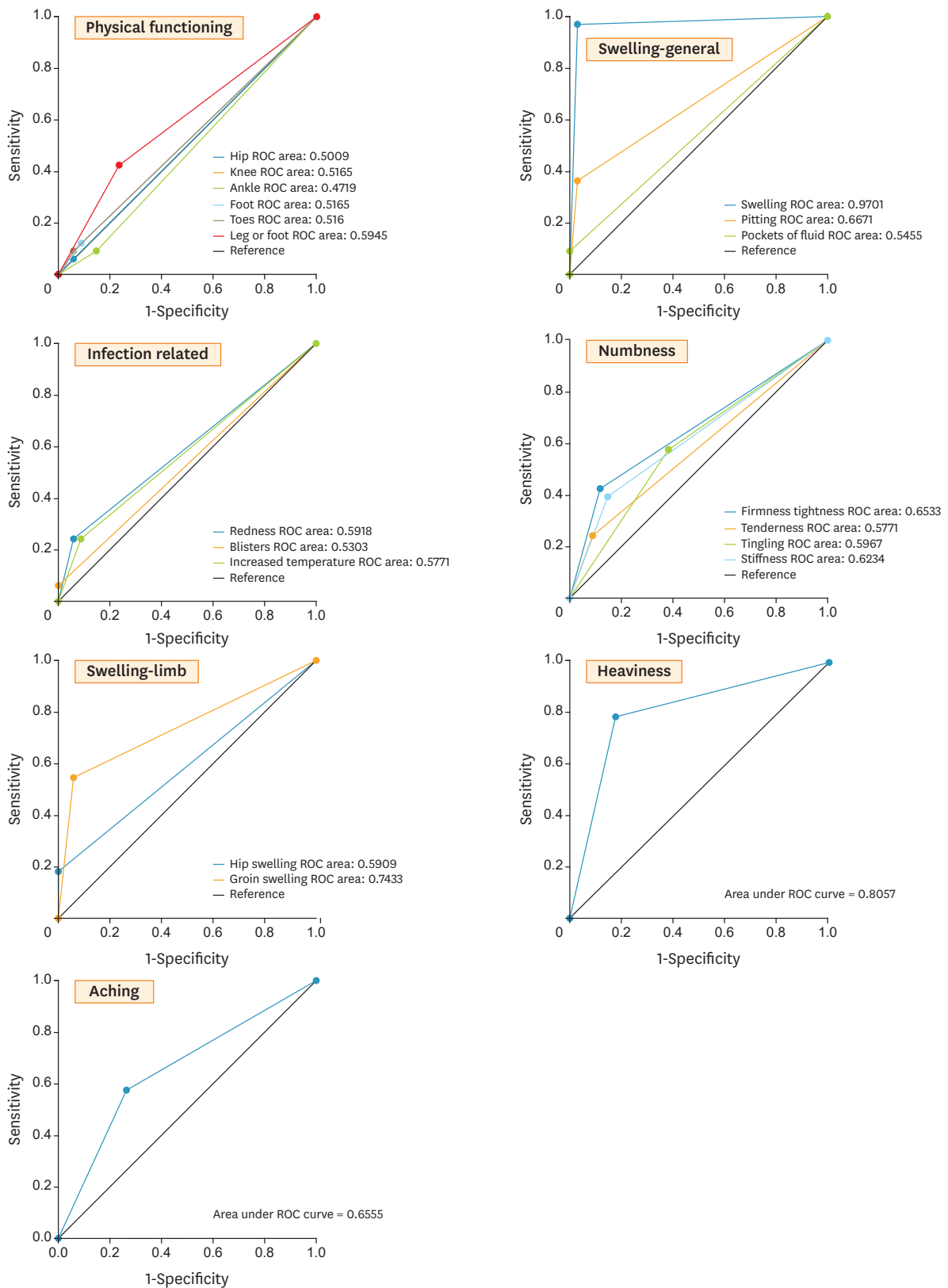
From among the 11 candidate items, the items for all 7 clusters were combined, and 12 possible models were constructed (**Table 2**). By comparing AUCs as well as sensitivity and specificity at their best cutoff values, Model 1 was identified as the best model and named GCLQ-7. This model exhibited an AUC of 0.945 (95% CI, 0.900–0.991), which is comparable with that of the original GCLQ-K (AUC, 0.867; 95% CI, 0.779–0.956; **Fig. 2**). The best cutoff value was 2 points in the GCLQ-7 model, and at this value, the sensitivity and specificity were 97.0% and 76.5%, respectively. Cronbach’s  $\alpha$  for GCLQ-7 was 0.699, showing a questionable reliability as compared with that of the original GCLQ-K was 0.829 [11].

**Table 1.** Selection of items from the original GCLQ-K

Symptom cluster	Item No.	Original GCLQ-K	Candidate	GCLQ-7
Physical functioning	1	Limited movement of your hip		
	2	Limited movement of your knee	V	V
	3	Limited movement of your ankle		
	4	Limited movement of your foot		
	5	Limited movement of your toes		
	6	Leg or foot feels weak	V	
Swelling-general	8	Experienced swelling	V	V
	9	Experienced swelling with pitting		
	20	Experienced pockets of fluid		
Infection-related	10	Experienced redness	V	V
	11	Experienced blistering		
	13	Experienced increased temperature in the leg	V	
Numbness	12	Experienced firmness/tightness	V	V
	7	Experienced tenderness		
	15	Experienced numbness	V	
	16	Experienced stiffness	V	
Swelling-limb	18	Experienced hip swelling		
	19	Experienced groin swelling	V	V
Heaviness	14	Experienced heaviness	V	V
Aching	17	Experienced aching	V	V

GCLQ, Gynecologic Cancer Lymphedema Questionnaire.

Development of the short version of the GCLQ



**Fig. 1.** ROC curves of the individual GCLQ-K items grouped according to symptom cluster. ROC, receiver-operating characteristic; GCLQ, Gynecologic Cancer Lymphedema Questionnaire.

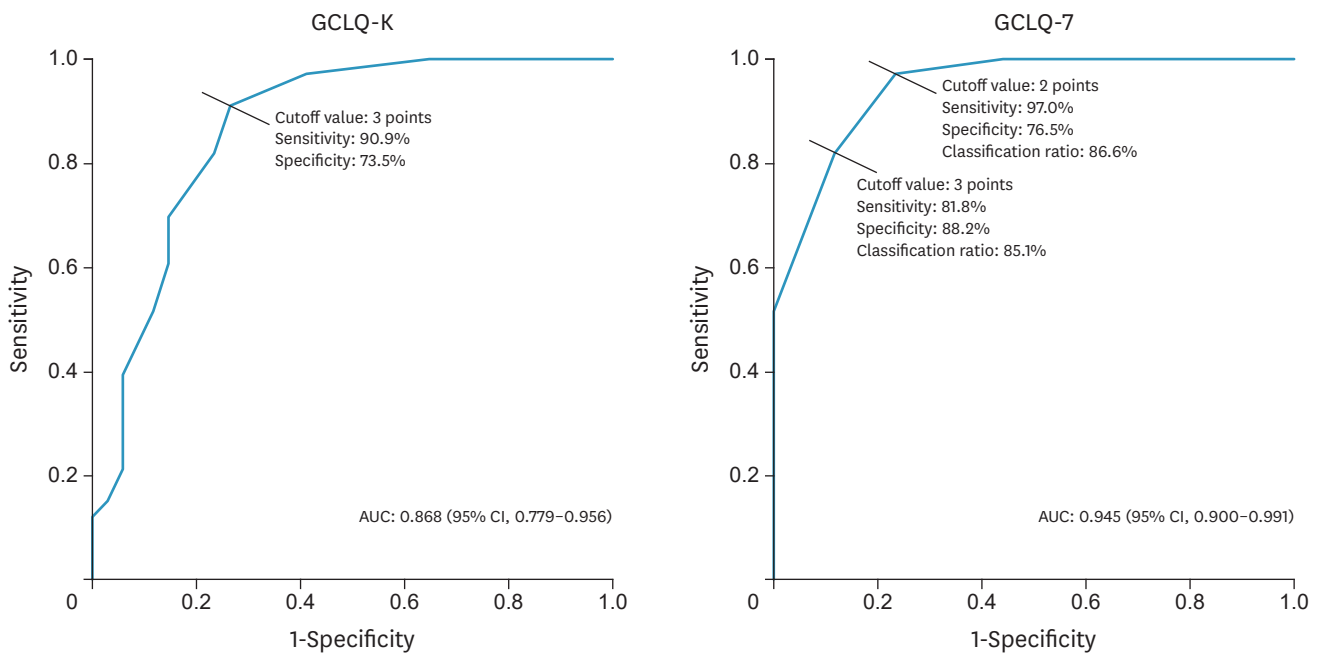
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**Table 2.** Possible models constructed from the candidate items

Symptom cluster	Model											
	1	2	3	4	5	6	7	8	9	10	11	12
Swelling-general	#8 (swelling)											
Swelling-limb	#19 (groin swelling)											
Heaviness	#14 (heaviness)											
Aching	#17 (aching)											
Physical functioning	#2 (limited knee movement)						#6 (leg or foot weakness)					
Infection-related	#10 (redness)			#13 (increased temperature)			#10 (redness)			#13 (increased temperature)		
Numbness	#12 (firmness/ tightness)	#15 (numbness)	#16 (stiffness)	#12 (firmness/ tightness)	#15 (numbness)	#16 (stiffness)	#12 (firmness/ tightness)	#15 (numbness)	#16 (stiffness)	#12 (firmness/ tightness)	#15 (numbness)	#16 (stiffness)
AUC	0.945	0.926	0.933	0.941	0.921	0.930	0.935	0.915	0.924	0.934	0.910	0.921
Sensitivity* (%)	97.0	97.0	97.0	84.8	87.9	97.0	97.0	84.8	97.0	87.9	87.9	97.0
Specificity* (%)	76.5	76.5	79.4	91.2	88.2	79.4	76.5	88.2	79.4	91.2	85.3	76.5

AUC, area under the curve of the receiver-operating characteristic curve.

\*Values at the best cutoff value in each model.



**Fig. 2.** Comparison of the ROC curves between the original GCLQ-K and GCLQ-7.

ROC, receiver-operating characteristic; GCLQ, Gynecologic Cancer Lymphedema Questionnaire; AUC, area under the curve.

## DISCUSSION

In the present study, the reliable short version model of GCLQ-K was successfully developed. Judging from the ROC curve studies, this model showed acceptable discrimination ability as compared with the original GCLQ.

It is interesting that the original GCLQ-K showed relatively low AUC (0.867) in our study population [11]. One of the possible reasons for this might be the questionnaire itself. The GCLQ-K is composed of 20 diverse items, and each item assesses whether or not the patient has specific symptoms (e.g., limited movement, swelling, or numbness) at a specific site (e.g., hip, knee, or ankle). Some of these items might have poor discrimination ability. By

contrast, the newly developed GCLQ-7 comprises of “key” questions alone that represent individual symptom clusters and might better distinguish patients with LLL.

Development of a short version of the questionnaire is important. Some widely-used questionnaire tools that measure QOL of patients with cancer consist of too many question items (e.g., a total of 30 items for the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30) [13]. The large number of items might facilitate detailed assessment for specific topics. However, from the subjects’ point of view, a long and complex questionnaire set takes a long time to complete, which might lower the subjects’ concentration level, and the completeness and reproducibility of the survey. In addition, for early detection of disease and monitoring treatment, a short version of the questionnaire would be necessary and much useful. For these reasons, several studies developed short versions of preexisting questionnaire tools. The Female Sexual Function Index (FSFI), which measures women’s sexual dysfunction, is one example of these efforts. The original FSFI was a 19-item self-reported questionnaire set [14]. Although it was one of the most powerful and useful diagnostic tools, Isidori et al. [15] recognized that it was too long for routine use in overcrowded outpatient clinics and developed and validated a 6-item version of FSFI. From then on, the FSFI-6 has been widely used in both clinical and research fields.

The present study has several methodological limitations. First, in the item selection, we tried to choose the best performing item in each symptom cluster. However, the AUCs of the ROC curves for the individual items did not differ so much in some symptom clusters (physical functioning, infection-related, and numbness clusters), resulting in a total of 12 possible models.

Second, in the model selection, the AUCs of the ROC curves for individual models were solely considered. If the best model was chosen based on the combination of the items having the largest AUCs alone within the 7 symptom clusters, it would be Model 7. In fact, Model 1 (GCLQ-7) and Model 7 showed similar ROC curves and not so different AUCs (0.945 vs. 0.935). This lack of marked differences might suggest that just combination of the existing items is not sufficient: modifying a single item question and/or combining two or three item questions would be necessary for better discrimination performance.

Third, correlations between the items within the same symptom clusters and those of different clusters were not considered. For example, 2 candidate items of the same physical functioning cluster were “limited knee movement (item 2)” and “leg or foot weakness (item 6).” While item 2 indicates only the specific site, item 6 indicates a much broader site. In the swelling-general cluster, “swelling (item 8)” precedes “swelling with pitting (item 9),” chronologically reflecting the clinical manifestations of LLL [16]. Another example is that “swelling (item 8)” of the swelling-general cluster is indeed related with “limited knee movement (item 2)” of physical functioning [7,17]. Muscle weakness also may mediate this relationship between swelling and limited movement. Thus, both temporal and causal relationships among the items should be considered. The clinical manifestations of LLL and the anatomical movement of the leg should also be considered.

Fourth, the cutoff GCLQ-7 score is also controversial. From the statistical analyses, we selected 2 points in this study. However, the classification ratio was not so different between the cutoff values of 2 and 3 points (86.6% vs. 85.1%, respectively). This means that accuracy would be similar whether the cutoff value was 2 or 3 points (**Fig. 2**). At the same time, the



risks of false-positive and false-negative rates should be weighed in the selection of cut off values. Both sensitivity and false-positive rate were relatively higher when the cutoff score was 2 points than when the cutoff score was 3 points. The balance between a false-positive rate and a false-negative rate might also be affected by individual clinical conditions such as early detection or follow-up during treatment. These points should be considered in the future development of the GCLQ-7.

Lastly, the number of the study population in this retrospective cohort study was small (n=67). This aspect might affect both process of item selection and process of model selection. As the GCLQ-7 has the fewer number of items compared to the original version, prospective cohort studies with larger sample size is necessary to prove and validate its efficacy as a diagnostic tool.

In conclusion, the present study could newly develop the short version model of the GCLQ-K with acceptable ability to discriminate patients with LLL from those without LLL as that of the original version. In the near future, the GCLQ-7 will be modified based on the Delphi method by experts in gynecologic oncology, rehabilitation medicine, and lymphology. The version containing better clinical perspectives is expected in this step. The final version will be validated prospectively in case and control groups.

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