JGO 2017 Workshop for Good Authors & Reviewers:

How to prepare/write your investigation for publication

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Associate editor of JGO

Basic triad of an original article

- A subject worth reporting:
  - Ensure not repeating what has been done successfully before

- Knowledge of the basic structure of a peer-reviewed article

- Knowledge of the essentials of good writing
  - Original
  - Honest
  - Innovative
  - Organized
  - Careful
  - Clear
  - Modest
  - Fair-minded
  - Frank
  - Persistent
  - Rigorous
  - Realistic

BE ORIGINAL!

Article structure and Writing sequence

- Title page
- Abstract
- Introduction
- Methods
- Results
- Discussion
- Conclusions
- Acknowledgements
- References
- Tables and table captions
- Figures and figure legends
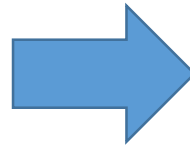
- Methods
- Figures and tables
- Results
- Introduction
- Discussion
- Abstract
- Conclusions

Standards for different types of articles
(https://www.ejgo.org/index.php?body=guideline)

JOURNAL OF GYNECOLOGIC ONCOLOGY

2015 Impact Factor
2.522

JGO Journal Metrics
CiteScore
1.99
SCImago Journal Rank (SJR)

Standards for Different Types of A...

Following guidelines for five different types of articles have been adopted by the *Journal Of Gynecologic Oncology*:

Investigators who are planning, conducting, or reporting randomized trials, meta-analyses of randomized trials, ...vational studies, observational studies, or studies of diagnostic accuracy should be familiar ...dards and follow these guidelines in articles submitted for publication.

CONSORT 📄
(Consolidated Standards of Reporting Trials) standards for reporting randomized trials

PRISMA 📄
(Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines for reporting systematic reviews and meta-analyses

MOOSE 📄
...Observational Studies in Epidemiology) guidelines for meta-analyses and systematic reviews of ...ies

STROBE 📄
(Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for the reporting of observational studies

STARD 📄
(Standards for Reporting of Diagnostic Accuracy) standards for reporting studies of diagnostic accuracy

REMARK 📄
REporting recommendations for tumor MARKer prognostic studies (REMARK)

SQUIRE 📄
(Standards for Quality Improvement Reporting Excellence) guidelines for quality improvement in health care

CHEERS 📄
(Consolidated Health Economic Evaluation Reporting Standards) statement for economic evaluations of health interventions

COREQ 📄
(Consolidated criteria for Reporting Qualitative research) for qualitative research interviews and focus groups

SAMPL 📄
(Statistical Analyses and Methods in the Published Literature) guidelines for basic statistical reporting for articles published in biomedical journals

재료 및 방법
(Material & Methods)

What did I do?

재료(대상) 및 방법 작성의 개요

- "아무리 자세해도 지나치지 않다"

  - As explicit as possible by providing enough detail and references

- Purpose of MM

  - To allow other researchers to evaluate and repeat your work

  - 다른 연구자가 이 연구를 평가하고 <u>재현할 수 있도록 자세하게</u>

  - "like a recipe"

Methods (STROBE)

Study design	Present key elements of study design early in the paper
Setting	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	(a) Cohort study-give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. (b) Case-control study-give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of case and controls. (c) Cross-sectional study-give the eligibility criteria, and the sources and methods of selection of participants.
Variables	Cleary define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.
Data sources/measurement	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods of there is more than one group.
Bias	Describe any efforts to address potential sources of bias.
Study size	Explain how the study size was arrived at.
Quantitative variables	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.
Statistical methods	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (cohort study)/how matching of cases and controls (case-control study)/analytical methods taking account of sampling strategy (cross-sectional study)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	

재료 및 방법 기술의 지침

1. 훈련된 연구자라면 연구를 재현하기에 충분한 내용과 참고문헌을 기술하되, 불필요한 세부사항을 포함하지 않는다.

2. 재료 및 방법 이외에 결과를 포함하지 않는다.

3. 긴 설명이 필요한 세부사항은 부록을 활용한다.

4. 적절한 주제 또는 소주제 별로 내용을 정렬한다.

5. 새로운 주제는 적절한 신호를 사용하여 연결한다.

6. 기능이 명확하지 않은 실험절차는 그 목적을 설명한다.

7. 수동태가 바람직하다.

8. 뚜렷한 이유 없이 관점을 바꾸지 않는다.

9. 정확한 단어를 사용한다.

10. 윤리 지침을 따르고, 이에 대해 기술한다. (animal & clinical)

- If your method has previously been published and is well-known, then you should provide only the literature reference.
  - Stem cells were isolated, according to Johnson [23].
- If your method is unpublished, then you need to make sure you provide all essential details.
  - Stem cells were isolated using biotinylated carbon nanotubes coated with anti-CD34 antibodies.

관점(Point of view)

- 수동태가 많이 쓰임

  - Materials & methods 강조하기 위해

  - 글의 활력을 주기 위해 능동태를 한 번 정도 사용하기도 한다.

  > We collected the different fungal species from various tepuis in Venezuela.
  > Different fungal species were collected from various tepuis in Venezuela.

- 이유 없이 관점을 바꾸지 마라.

  - The assays were performed for 10 min at room temperature. We then added 10 ml of 95% ethanol.

  - The assays were performed for 10 min at room temperature. The 10 ml of 95% ethanol were added.

재료(대상)의 채택기준 및 제외기준

- Inclusion criteria

  the cervical smear collected before radiotherapy in 169 patients with stage IB1 through stage IVB cervical cancer (International Federation of Gynecology and Obstetrics [FIGO]) between July 2003 and December 2006, at the National Cancer Center, Goyang, Gyeonggi, Korea.

- Exclusion criteria

  Exclusion criteria included neuroendocrine histology, pathologically proven distant metastasis, history of psychiatric disease, preoperative urinary dysfunction, and another coexisting malignancy.

재료(대상) 선정방법, 규모 및 과정

- 연구에 사용한 개체 수(n)는 정확히 기록

- 시제는 과거를 주로 사용

  - "연구결과가 논문 중에 어떻게 기술되어 있다."라고 할 때는 현재 시제

  > *… Data are summarized as mean $\pm$ SD in Table 1…..*

- 이용된 대조군 기술

- 환자를 표현할 때는 patient A, B… 등으로 표현

- CONSORT statement : for RCT

  - Consolidated Standards of Reporting Trials

  - Checklist of essential item and flow diagram

- PRISMA statement : for systematic review and meta-analysis

  - Checklist and flow chart

동물, 약제, 시료, 기구 등의 기술

- Generic name 사용
  - Paclitaxel, dopamine HCl
  - 시약은 화학명
  - 괄호
    - 상품명, 제조회사명, 제조일시, 제조번호
    - 기계, Kit : 회사이름, 소재도시명, 나라이름
    - 체중, 농도, 용량 등은 괄호로 넣거나, 앞으로 가면 괄호 없이 기술

  > *DMEM culture medium (Gibco BRL, Long Islands, NY)*

  > *10 mg nitoglycerine , nitroglycerine (10 mg)*

- 동물을 사용할 경우, 어떤 실험동물과 연령을 정확히 기술
  - **<u>Animal (X)</u>**
  - Six weeks old female athymic nude mouse….
- 측정단위 : SI Unit

데이터분석

- 어떻게 변수를 계산하였는지

- 데이터를 어떻게 요약하였는지

  - 정규분포: 평균값과 표준편차

  - 비정규분포

    - 중앙값(median)과 범위(range)

    - 중앙값(median)과 사분위수범위(range between the 25th and the 75th percentiles)

통계 분석

- 잘 알려진 방법: 통계 방법만 기술.

  - Student t-test, Chi-square, ANOVA, linear regression, correlation, Wilcoxon

- 잘 알려지지 않은 통계 방법:

  - 논문이나 책을 참고문헌으로 제시

- 사용한 프로그램 (version, release number 포함)

- 각 통계 방법마다 샘플 크기가 다른 경우, 분명하게.

- 유의한 p 값 또는 95% 신뢰구간

결과
(Results)

What did I find?

결과 작성의 전략

- Use past tense
  - " Within 6 months of withdrawal, DTA decreased by 20 ± 6%."

- 표와 그림을 잘 구성하고, 활용

  - *Tables give the evidence and figures illustrate the highlights.*

- 결과부분은 소제목 (subheadings) 을 활용

- 각 부제목에서 각 표와 그림의 부분을 설명하고, 해당하는 표와 그림을 표기

  - *Introduce each group of tables and figures in a separate paragraph where the overall trends and data points of particular interest are noted.*

결과 작성의 전략

- 각 소제목에서 각 표와 그림을 언급하여 설명하되, 표와 그림의 내용을 반복하는 것은 최소화

  - *Be sure to include basic descriptive data.*

  - *The text should tell the story.*

- 각 결과가 재료와 방법에서 언급된 연구방법에 의한 결과임을 확인

- Indicate specific statistics including key statistics such as:

  - Number of samples

  - Index of dispersion: SD, SEM

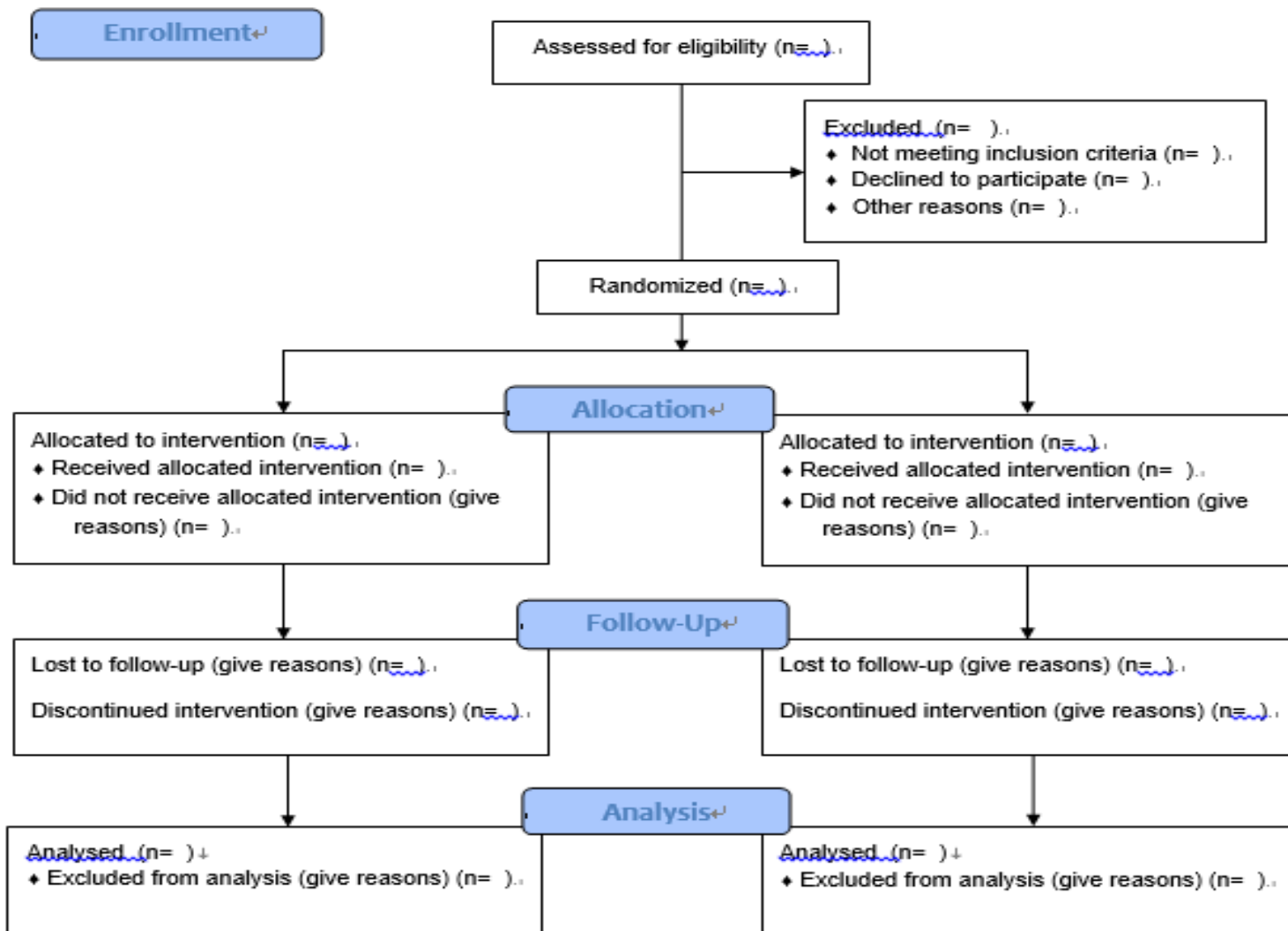 - Index of central tendency: mean, median or mode

Results (STROBE)

Participants	(a) Report the numbers of individuals at each stage of the study (eg. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed) (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	(a) Give characteristics of study participants (eg, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Cohort study - summarize follow-up time (eg, average and total amount)
Outcome data	Cohort study-Report numbers of outcome events or summary measures over time Case-control study-Report numbers in each exposure category, or summary measures of exposure Cross-sectional study-Report numbers of outcome events or summary measures
Main results	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg. 95% confidence interval). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.
Other analyses	Report other analyses done-eg. Analyses of subgroups and interactions, and sensitivity analyses

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	
	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram

Enrollment

Assessed for eligibility (n=)

Excluded (n=)
- ♦ Not meeting inclusion criteria (n=)
- ♦ Declined to participate (n=)
- ♦ Other reasons (n=)

Randomized (n=)

Allocation

Allocated to intervention (n=)
- ♦ Received allocated intervention (n=)
- ♦ Did not receive allocated intervention (give reasons) (n=)

Allocated to intervention (n=)
- ♦ Received allocated intervention (n=)
- ♦ Did not receive allocated intervention (give reasons) (n=)

Follow-Up

Lost to follow-up (give reasons) (n=)

Discontinued intervention (give reasons) (n=)

Lost to follow-up (give reasons) (n=)

Discontinued intervention (give reasons) (n=)

Analysis

Analysed (n=)
- ♦ Excluded from analysis (give reasons) (n=)

Analysed (n=)
- ♦ Excluded from analysis (give reasons) (n=)

Wordiness (장황함)

- Should not include irrelevant and peripheral information, including overview sentences
  - To show our results, we first introduce all components of experimental system and then describe the outcome of infections.
- Avoid adverbial intensifiers
  - "Clearly", "essential", "quite", "basically", "rather", "fairly", "really", "virtually"
  - not only add verbosity to your sentences, but also lower your results' credibility
- Avoid abstract nominalizations
  - We tested the hypothesis that there is a disruption of membrane asymmetry.
    - => We tested the hypothesis that membrane asymmetry is disrupted.
  - In this paper we provide an argument that stem cells repopulate injured organs.
    - => In this paper we argue that stem cells repopulate injured organs.

Mistakes to avoid

- This sections lend itself to overwriting, to underwriting, and to giving weight to non-significant results.

- Don't include just % or p value.
  - *Include confidence interval.*

- 'What might it mean' dealt in discussion section.
  - *Avoid beginning to discuss the implications or strengths and weaknesses of your study*
  - *Exception: aid in transition*

    "The results of the previous experiment suggested to us that the do pamine released was not derived from vesicular stores but from the cytoplasm. To test this possibility…"

"The effect on body weight was discussed."

"Body weight was increased."

"Body weight increased 43 ± 2% over a 6-day period."

서론
(Introduction)

Why is this paper important?

Why did I do it?

Introduction (STROBE)

Background /rationale	Explain the scientific background and rationale for the investigation being reported
Objective	State specific objectives, including any prespecified hypotheses

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Methods			
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Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	

Before moving on to create Introduction

- Methods 와 results 를 작성하면서, 많은 경우 original outline 에서 벗어나서 생각의 초점이 변경됨.

- 따라서, Methods and Results sections 을 다시 읽고, outline 을 다시 research focus 와 일치시키는 것이 필요함.

  - Review the general picture of your paper, topic, main idea, and purpose

Moves in Introduction

- Move 1. establish a research territory
  - Show that the general research area is important, central, interesting, and problematic in some way;
  - Introduce and review items of previous research in the area.
- Move 2. find a niche
  - Indicate a gap in the previous research, or extend previous knowledge in some way.
- Move 3. occupy the niche
  - Outline purposes or state the nature of the present research;
  - List research questions or hypotheses;
  - Announce principle findings;
  - State the value of the present research;
  - Indicate the structure of the research paper.

Kallenstinova. Yale J Biol Med. 2011

서론 작성 시 주의점

- 간결하게!! 짧고 명료하게 작성 (250-600 words)

- 단도직입적

- 무엇에 의문을 느끼고 연구를 시작하였는지 금방 알아차릴 수 있도록

- 결과나 결론과 직접 관련이 없는 장황한 교과서적 배경 설명 배제

- 가치가 있는지? 누가 읽을 것인지? 발표하기에 적합한 학술지는 어느 것 인지?

- 문장의 시제
  - 현재형: 명확히 알려진 사실
  - 과거형: 최근 연구된 내용이나 추가적인 연구가 필요한 결과, 타 연구와 배치되는 결론 등

Mistakes to avoid

- Don't just describe the substance or problem under study

- Don't try to show readers that you have read everything

- Do not include your fascinating work that is tangential or barely related to the central topic.

- Avoid formulaic first lines

  - "Addiction to "x" is a significant health problem"

  - "Access to legalized gambling has increased in the last two decades"

Discussion

Discussion (STROBE)

Key results	Summarize key results with reference to study objectives
Limitations	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Generalisa bility	Discuss the generalizability (external validity) of the study results

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Purpose of discussion section

- To place your findings in the research context
- To explain the meaning of the findings and why they are important, without appearing arrogant, condescending, or patronizing.

- A mirror reflection

- Introduction
  - Move 1. establish a research territory
  - Zoom in
    - From general to specific
    - From the background to your research question

- Discussion
  - Move 1. the study's major findings
  - Move 2. research context
  - Zoom out
    - From the summary of your findings to the research context

Moves in discussions

- Move 1. The study's major findings
  - State the study's major findings.
  - Explain the meaning and importance of your findings.
  - Consider alternative explanations of the findings.

- Move 2. Research Context
  - Compare and contrast your findings with those of other published results.
  - Explain any discrepancies and unexpected findings.
  - State the limitations, weaknesses, and assumptions of your study.

- Move 3. Closing the paper
  - Summarize the answers to the research questions.
  - Indicate the importance of the work by stating applications, recommendations, and implications.

Kallenstinova. Yale J Biol Med. 2011

Opening paragraph of discussion section

- The biggest challenge for many writers
- Best choice
  - To start with the study's major findings that provide the answer to the research question in your Introduction
  - Examples,
    - "Our findings demonstrate….."
    - "In this study, we have shown that…."
    - "Our results suggest….."

Improvements to the FIGO staging for ovarian cancer: reconsideration of lymphatic spread and intraoperative tumor rupture

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CONFLICT OF INTEREST

Dong Hoon Suh and Jae-Weon Kim serve as Editors of the JGO but have no role in the decision to publish this article. No other conflict of interest relevant to this article was reported.

MATERIALS AND METHODS

Data were obtained from the review of the medical charts of all patients with epithelial ovarian, fallopian tube, and primary peritoneal cancers at three Seoul National University-affiliated hospitals between 1990 and 2011. Each of the Institutional Review Boards of the three hospitals approved this study. Data on patient demographics, primary cancer sites, stages, grades, histology, first courses of treatment, intraoperative findings regarding tumor spread, operation procedures performed, residual disease, adjuvant chemotherapy, recurrence, and survival were collected. Optimal cytoreduction was defined as a residual tumor size of <1 cm. A total of 870 patients were eligible for analysis, as shown in **Fig. 1**.

Stages were reassigned according to the following criteria when indicated: surgical spillage with intraoperative tumor rupture (IC1), capsule rupture before surgery or presence of a tumor on the surface (IC2), and presence of malignant cells on ascites or peritoneal washing cytology (IC3); microscopic (IIB1) and macroscopic (IIB2) pelvic spread; microscopic extrapelvic spread (IIIA1) and retroperitoneal LN metastasis without extrapelvic spread (IIIA2); and supraclavicular LN metastasis (IVA) and other distant metastasis (IVB).

Kaplan-Meier survival estimates were derived for overall survival (OS) both before and after stage reassignment. Univariate and multivariate analyses were performed using Cox proportional hazards models in order to evaluate the association between the site of distant metastasis and OS outcomes. Various prognostic factors for the sub-stages were also compared using the chi-square test, Student's t-test, and Kruskal-Wallis test, as appropriate, to assess the association of these factors with survival outcomes. The OS rates were defined as duration from the date of diagnosis to either the recorded date of death from ovarian cancer or the date of death provided by Statistics Korea. Statistical tests were 2-sided, with $p < 0.05$ indicating significance. Statistical analyses were performed using SPSS ver. 19.0 (IBM Co., Armonk, NY, USA).
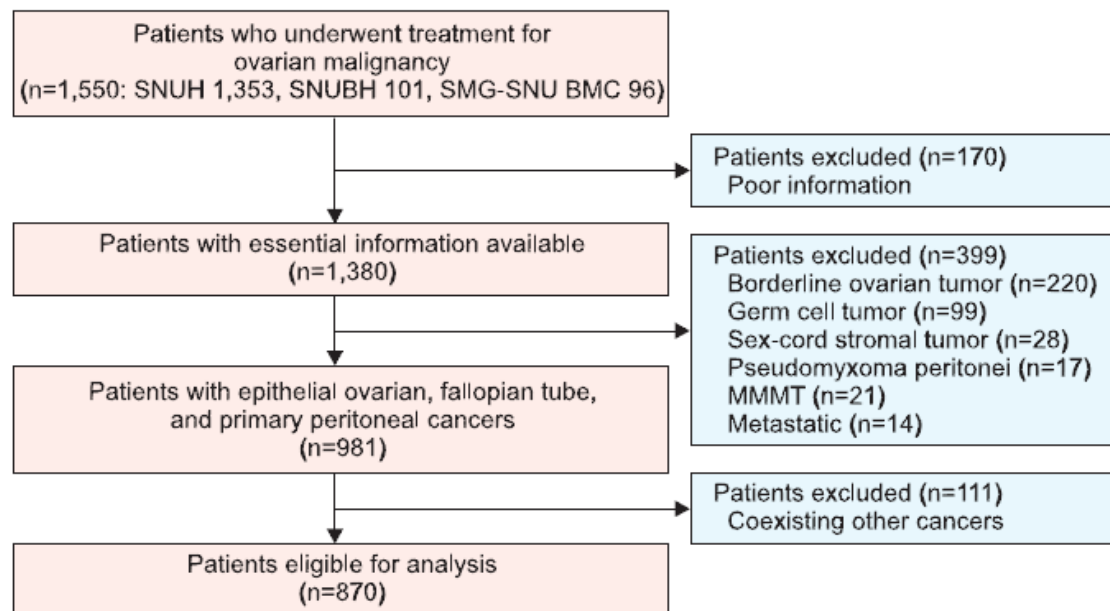
- Participants and data sources
- Variables with definition
- Study setting for comparison
- Statistical methods

Fig. 1. Patient enrollment. SNUH, Seoul National University Hospital; SNUBH, Seoul National University Bundang Hospital; SMG-SNU BMC, Seoul Metropolitan Government-Seoul National University Boramae Medical Center; MMMT, malignant mixed mullerian tumor.

Table 1. Patient characteristics and treatment outcomes (n=870)

Characteristic	No. (%)
Age at diagnosis (yr), mean±SD	51.7±12.8
Primary cancer site	
Ovary	846 (97.2)
Fallopian tube	12 (1.4)
Peritoneum	12 (1.4)
FIGO stage	
I	254 (29.2)
II	56 (6.4)
III	483 (55.5)
IV	77 (8.9)
Histology	
Serous	494 (56.8)
Non-serous	376 (43.2)
Grade	
I	97 (11.2)
II and III	484 (55.6)
Unknown	289 (33.2)
Initial serum CA-125 level (U/mL)	
≥35	143 (16.4)
<35	668 (76.8)
Unknown	59 (6.8)
Neoadjuvant chemotherapy	84 (9.7)
Lymphadenectomy	
Stage I and II (n=310)	100 (32.3)
Stage III and IV (n=560)	183 (32.7)
Residual tumor size < 1 cm	
Stage I and II (n=310)	301 (97.1)
Stage III and IV (n=560)	316 (56.4)
Recurrence	450 (51.7)
Progression-free survival (mo), median (range)	18 (0 to 247)
5-yr overall survival rate (%)	56.5

FIGO, International Federation of Gynecology and Obstetrics.

Table 2. Stage migration after stage reassignment and corresponding 5-year overall survival rates (5YSR)

Current staging	5YSR (%)	IA	IB	IC1	IC2	IC3	IIA	IIB1	IIB2	IIC	IIIA1	IIIA2	IIIB	IIIC	IVA	IVB	Total
		93.5	NC	92.0	85.0	71.0	NC	70.0	76.0	74.5	57.5	66.3	54.0	35.8	52.0	28.0	56.5
IA	93.5	128															128
IB	NC		7														7
IC	82.5			39	27	53											119
IIA	NC						6										6
IIB	75.0							11	21								32
IIC	74.5									18							18
IIIA	57.5										12						12
IIIB	54.0												61				61
IIIC	38.5											33		377			410
IV	33.0														17	60	77
Total	56.5	128	7	39	27	53	6	11	21	18	12	33	61	377	17	60	870

IC1, intraoperative tumor rupture; IC2, capsule ruptured before surgery or tumor on surface; IC3, malignant cells in the ascites or peritoneal washings; IIB1, microscopic pelvic spread; IIB2, macroscopic pelvic spread; IIIA2, retroperitoneal lymph node metastasis without extrapelvic involvement; IVA1, supraclavicular lymph node metastasis; IVB2, distant metastasis other than supraclavicular lymph node; NC, not calculated due to small patient number.

Table 3. Univariate and multivariate analyses of the site of distant metastasis as a function of overall survival in stage IV ovarian cancer (n=77)

Site of distant metastasis	No. (%)	Multiple sites ≥ 2, no. (%)	Overall survival (mo), median (range)	Univariate analysis, HR (95% CI)	Multivariate analysis	
					HR (95% CI)	p-value
Pleural effusion	36 (46.8)*	8 (22.2)	31 (1–198)	1.01 (0.58–1.77)	0.54 (0.26–1.10)	0.090
Liver parenchyma	24 (31.2)	13 (54.2)	38 (1–91)	1.19 (0.66–2.14)	0.64 (0.30–1.34)	0.237
Supraclavicular LN	17 (22.1)	7 (41.2)	46 (6–162)	0.34 (0.13–0.85)	0.22 (0.08–0.63)	0.005
Lung	14 (18.2)	13 (92.9)	22 (1–54)	1.65 (0.79–3.45)	1.44 (0.61–3.36)	0.404
Bone	13 (16.9)	12 (92.3)	20 (1–57)	1.93 (0.89–4.17)	3.49 (1.10–11.08)	0.034
Brain	11 (14.3)	10 (90.9)	57 (1–143)	1.02 (0.42–2.40)	0.33 (0.11–1.02)	0.053

HR, hazard ratio; CI, confidence interval; LN, lymph node.
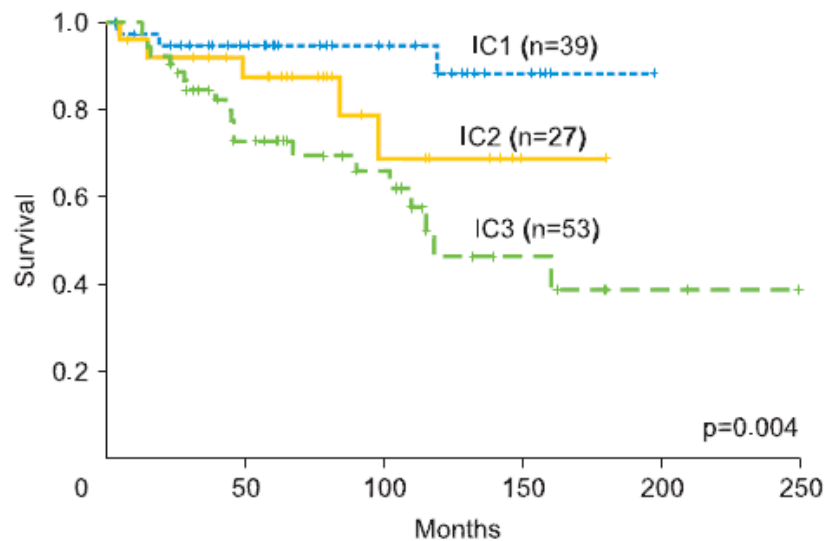*Three were not pathologically confirmed.

Fig. 2. Overall survival of patients with stage IC ovarian cancer according to reassigned stages. IC1, intraoperative tumor rupture; IC2, capsule ruptured before surgery or tumor on surface; IC3, malignant cells in the ascites or peritoneal washings.
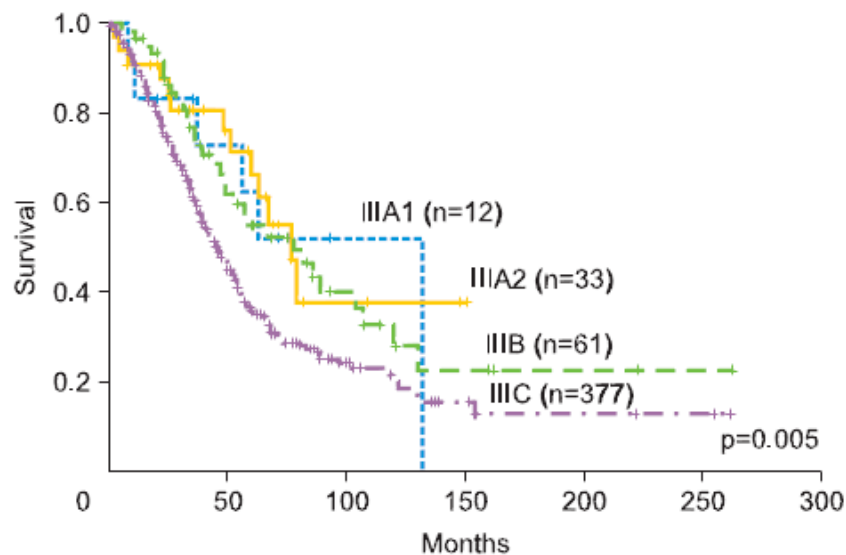

Fig. 3. Overall survival of patients with stage III ovarian cancer according to reassigned stages. Retroperitoneal lymph node metastasis without extrapelvic involvement was downstaged from stage IIIC to IIIA2.
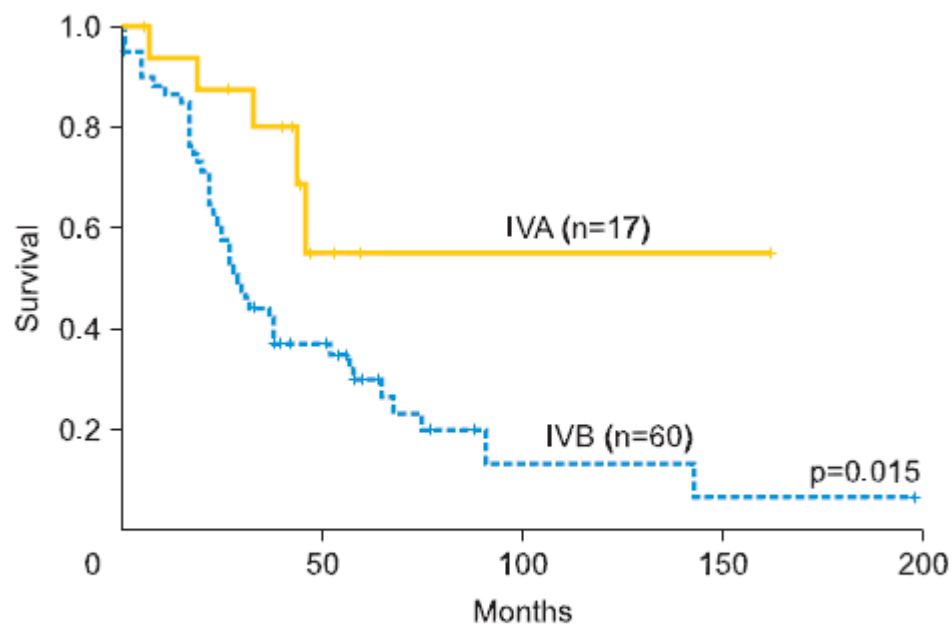

Fig. 4. Overall survival of patients with stage IV ovarian cancer according to sub-staging. Supraclavicular lymph node metastasis (stage IVA) vs. other sites metastasis (stage IVB).

INTRODUCTION

Among gynecologic malignancies, ovarian cancer is the leading cause of cancer-related deaths [1]. The International Federation of Gynecology and Obstetrics (FIGO) staging for ovarian cancer reflects the prognosis of affected patients. The current staging was accepted by FIGO in 1988. However, many studies have indicated the necessity of a revision of the current FIGO staging guidelines for better prognostic discrimination. For stage IC disease, a growing body of evidence suggests that intraoperative rupture might not increase the risk of tumor recurrence [2,3]. For stage IIB disease, macroscopic pelvic peritoneal tumor masses might be associated with poor survival outcomes compared with microscopic tumor infiltration or adherence [4]. Many studies have reported better prognosis for stage IIIC ovarian cancer with lymph node (LN) involvement alone (without peritoneal carcinomatosis) than with LN involvement and concomitant peritoneal carcinomatosis [5-7]. The revision process is currently underway by the Gynecology Oncology Committee of FIGO in collaboration with various international societies and agencies, and the revision would be addressed about the stage IIIC classification, at least [8].

Since the revision process should be finalized only after a consensus is reached by all relevant international organizations through extensive consultations, we performed this timely study to evaluate whether the revision of FIGO sub-staging for ovarian carcinoma could improve prognosis prediction. Furthermore, the favorable prognosis of FIGO stage IIIC ovarian cancer characterized by LN-positive disease only, prompted us to compare the survival outcomes of stage IV disease so-assigned based on supraclavicular LN metastasis with those of stage IV disease so-assigned based on the other metastatic sites.

- Establish research territory

- Find a niche: problematic in some way

- Previous research addressing the problem

- Outline purposes

Our study demonstrates the necessity for revision of the current FIGO staging for ovarian cancer with regard to the 3 sub-staging issues for stages IC, III, and IV. The sub-staging process has 2 main implications. First, stage IC was sub-staged as stages IC1, IC2, and IC3, to account for the distinct prognoses associated with the etiology of tumor rupture. Second, considering the relatively favorable prognosis associated with lymphatic tumor spread compared with peritoneal tumor spread, stage IIIC, which was classified solely on the basis of LN metastasis, was down-staged to stage IIIA2. Similarly, stage IV was sub-staged as stage IVA, with distant metastasis to the supraclavicular LNs, and stage IVB, with other distant metastasis.

There has been much controversy regarding the cause of tumor rupture that upstages cancers to stage IC with regard to prognosis. Vergote et al. [9] demonstrated that tumor rupture during surgery (HR, 2.65; 95% CI, 1.53 to 4.56; p<0.001) and before surgery (HR, 1.64; 95% CI, 1.07 to 2.51; p=0.022) had an independent unfavorable impact on disease-free survival. However, other researchers failed to show that capsular rupture caused by the surgeon affected the prognosis of patients with early-stage ovarian cancer [3,10,11]. A recently published meta-analysis supported this finding and concluded that intraoperative rupture might not decrease progression-free survival compared to no rupture in early-stage ovarian cancer with complete surgical staging and adjuvant platinum-based chemotherapy [2]. This finding is consistent with our findings that the 5YSR of patients with sub-stage IC1 disease was similar to that of patients with stage IA disease and was clearly higher than that of patients with sub-stage IC3 disease.

Many studies have supported Berek's suggestion of a separate entity for LN-positive stage IIIC ovarian cancer [5-7]. Berek [5] argued that FIGO should consider modifying the ovarian cancer staging by further stratifying stage III disease on the basis of the better OS in patients with retroperitoneal LN metastasis without peritoneal carcinomatosis than in

patients with macroscopic peritoneal carcinomatosis. One plausible explanation for the favorable prognosis of those patients with sub-stage IIIA2 disease might be the higher optimal cytoreduction rate compared to the patients with stage IIIC disease showing intraperitoneal tumor implants >2 cm. Optimal cytoreduction was a well-known and important prognostic factor for advanced-stage ovarian cancer [12]. Our study also showed that optimal cytoreduction was an independent prognostic factor for OS in patients with stage III disease. Bachmann et al. [13] reported that the influence of LN metastasis on prognosis decreases with the increase in residual tumor volume. The authors also reported that the nodal status seemed to be the next most important prognostic factor for advanced-stage ovarian cancer. Additionally, successful retreatment of recurrence in patients upstaged to stage IIIC on the basis of LN metastasis alone with second surgery and chemotherapy could partly account for the favorable prognosis of these patients [6,14,15].

- Major findings
- Meaning and importance of your findings
- Compare and contrast your findings with those of other published results
- Plausible explanations with supporting evidences

The primary routes of ovarian cancer metastasis include intra-peritoneal implantation of exfoliated cells at distant sites and spreading through retroperitoneal lymphatic channels [16]. Spreading through the lymphatic channels of the diaphragm and the retroperitoneal LNs can lead to dissemination above the diaphragm, especially to the supraclavicular LNs [5]. In accordance with the favorable prognosis of LN-positive-only stage IIIC disease, stage IV disease, assigned on the basis of supraclavicular LN metastasis, might be associated with better survival outcomes than stage IV disease. Nevertheless, no study has investigated the favorable prognosis of stage IV ovarian cancer patients with supraclavicular LN metastasis. To the best of our knowledge, this study is the first one to demonstrate a distinctly better OS for stage IV ovarian cancer patients with supraclavicular LN metastasis than for patients with other forms of distant metastasis. Since ovarian cancer is known to spread both intraperitoneally and retroperitoneally almost simultaneously [17], the presence of tumor spreading mainly through lymphatic channels without intra-peritoneal dissemination suggests that such tumors might be associated with a favorable biologic behavior. In support of this idea, our study shows that sub-stage IVA disease was associated with a relatively limited number of simultaneous metastatic sites compared with sub-stage IVB disease. However, in this study, we failed to show any significant positive or negative associations between the prognosis of patients with sub-stage IVA disease and the prognostic factors that were already proven important for advanced-stage ovarian cancer, such as optimal cytoreduction and chemoresistance.

This study has some limitations. First, we did not show a significant difference in OS between sub-stages IIB1 and IIB2.

This might be partly due to the small number of patients with stage II disease. FIGO stage II ovarian cancer accounts for 8% of all ovarian cancers [4] and 6.4% in our study. Further studies with larger population numbers are needed in order to achieve sufficient statistical power. Second, the follow-up period for the study population was relatively short. This might result in an overestimation of the favorable prognosis of patients with stage IVA disease (5YSR, 52.0%), which was even better than that of patients with stage IIIC disease. A longer follow-up period could ensure that the survival estimates are more accurate. Third, the low rate of lymphadenectomy in early stage disease implicated that true pathologic stage IIIC disease could be included in the analysis of stage IC disease. However, the same result of a significant OS difference in stage IC patients who underwent staging lymphadenectomy was observed. Finally, mortality was not disease-specific but overall, without considering the cause of death. This might cause an underestimation of prognosis in this study. Nevertheless, the potential impact of this underestimation on the study results could be minimal because the age difference between the compared sub-stages was not significant.

In conclusion, modification of the current FIGO staging for ovarian carcinoma appears to improve the discrimination of the survival outcomes of patients with surgical spillage, retroperitoneal LN metastasis without extrapelvic peritoneal involvement, or distant metastasis to the supraclavicular LN. Further studies are warranted to explore the biologic mechanisms that underlie the favorable prognosis of patients with stage IV disease, so-assigned on the basis of supraclavicular LN metastasis.

Summary

- 논문의 전체 구성을 늘 생각하고 작성해야 한다.
  - 시작하여 단기간에 초고를 완성하는 것이 바람직하지만, 시간을 갖고 maturation 과정을 거치는 것이 좋다. '조금 지나서 다시 보면 이전에 보이지 않았던 오류나 미처 생각지 못했던 것들이 생각날 때가 있다.'
- Introduction에서 질문하고, 방법과 결과를 통해 근거를 제시하고, discussion에서 답을 하는 큰 흐름을 유지한다.
- 세세한 문법보다는 논리적인 문맥의 흐름에 집중한다. 단, confidence 강도를 결정하는 단어의 선택은 신중하게 (교정으로 바꿀 수 없는 부분들…)
- 게재를 원하는 저널을 미리 선정하고, 유사한 형식의 논문을 많이 읽어, 형식과 경향성을 파악하여 참조한다.

경청해주셔서 감사합니다.