AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Guideline on the Diagnosis and Treatment of Cervical Carcinoma

Published in February 2008 by the Working Group on Gynecological Oncology (*Arbeitsgemeinschaft für Gynäkologische Onkologie e.V,* AGO), affiliated to the German Cancer Society (*Deutsche Krebsgesellschaft e.V,* DKG) and the German Society for Gynecology and Obstetrics (*Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e.V.*, DGGG)

FORSCHEN
LEHREN
HEILEN

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Methodological report: S2k Guideline on Cervical Carcinoma

Guideline coordination:	Prof. M.W. Beckmann (Erlangen), AGO Prof. P. Mallmann (Cologne), DGGG
Guideline coordination AGO/DKG/DGGG:	Prof. M.W. Beckmann (Erlangen)
Project management DKG/AWMF:	Anita Prescher, B.Sc. Eng., DKG (Berlin)
Chair of the consensus procedure:	Dr. Ina Kopp, AWMF (Marburg)

Editorial committee:

Prof. Horn, Leipzig; Prof. Schmidt, Mannheim; Dr. Pilch, Frankenthal (adjunct professor); Prof. Kimmig, Essen; Dr. Haensgen, Halle (adjunct professor); Dr. Marnitz, Berlin (adjunct professor); Dr. Rein, Düsseldorf (adjunct professor)

Uterus Commission of the AGO:

Dr. Ackermann, Darmstadt (adjunct professor); Prof. Ebert; Prof. Hillemanns, Hanover; Prof. Höckel, Leipzig; Prof. Kleine, Freiburg; Dr. Köhler, Berlin (adjunct professor); Prof. Lampe, Leverkusen; Prof. Lichtenegger, Berlin; Prof. Loening, Hamburg; Dr. Rudlowski, Bonn (adjunct professor); Prof. Runnebaum, Jena; Prof. Schneider, Berlin; Prof. Schnürch, Neuss; Prof. Sommer, Munich; Dr. Strauss, Halle; Prof. Strnad, Erlangen; Prof. Ulrich; Dr. Weidner, Tübingen

FORSCHEN
LEHREN
HEILEN

AGO
ARBEITSGEMEINSCHAFT
GYNÄKOLOGISCHE
ONKOLOGIE E.V.
UTERUS KOMMISSION
© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Methodological report: key recommendations

In formulating the recommendations, three different qualities were distinguished whenever possible:

— "Must/must not," corresponding to a strong recommendation for/against an intervention

— "Should/should not," corresponding to a recommendation for/against an intervention

— "Can/may," corresponding to an optional action with some uncertainty

FORSCHEN
LEHREN
HEILEN

ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Methodological report: S2k guideline on cervical carcinoma

Specialist society/organization	Representative
Working Group on Psycho-Oncology (*Arbeitsgemeinschaft für Psychoonkologie,* PSO)	Prof. J. Weis Dr. M. Keller
Working Group on Gynecological Oncology (*Arbeitsgemeinschaft Gynäkologische Onkologie,* AGO)	Prof. M.W. Beckmann Prof. G. Emons
Working Group on Radiological Oncology (*Arbeitsgemeinschaft Radiologische Onkologie,* ARO)	Prof. G. Hänsgen
German Society for Radio-Oncology (*Deutsche Gesellschaft für Radioonkologie,* DEGRO)	Prof. W. Harms
Working Group on Rehabilitation, Follow-Up, and Social Medicine (*Arbeitsgemeinschaft Rehabilitation, Nachsorge und Sozialmedizin,* ARNS)	Prof. R. Schröck
Working Group on Supportive Measures (*Arbeitskreis Supportivmassnahmen,* ASO)	Prof. P. Feyer Dr. K. Jordan
Association of Gynecologists (*Berufsverband der Frauenärzte* e.V.)	Dr. K. König
German Society for Gynecology and Obstetrics (*Deutsche Gesellschaft für Gynäkologie und Geburtshilfe,* DGGG)	Prof. P. Mallmann Prof. R. Kimmig
Working Group on Oncological Pathology (*Arbeitsgemeinschaft onkologische Pathologie,* AOP)	Prof. D. Schmidt
German Society for Pathology (*Deutsche Gesellschaft für Pathologie,* DGP)	Prof. L.-C. Horn
German Radiology Society (*Deutsche Röntgengesellschaft,* DRG)	Prof. B. Hamm
Women's Self-Help after Cancer (*Frauenselbsthilfe nach Krebs* e.V.)	Ms. B. Reckers
Conference of Oncological and Pediatric Nurses (*Konferenz onkologischer Kranken- und Kinderkrankenpflege,* KOK)	Ms. K. Paradis

FORSCHEN
LEHREN
HEILEN

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Epidemiology

— The incidence of cervical carcinoma ranges from 3.6 (in Finland) to 45 (in Columbia) per 100,000 women per year. In Germany, the incidence is 13.3 per 100,000 women.

— The incidence of precancerous cervical lesions is around 100 times higher in comparison with cervical carcinoma — i.e., around 1% in Germany.

— In 2002, 6500 women developed cervical carcinoma in Germany, and more than 1700 women died of it.

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Prevention and early detection I

1. Primary prevention of cervical dysplasia and invasive carcinoma is possible by avoiding genital infection with human papillomavirus (HPV).
2. Consistent use of condoms reduces the risk of transmission of HPV infection.
3. General vaccination against human papillomavirus is recommended for all girls aged 12–17.
4. Regular examinations for early cancer detection are necessary.
5. Secondary prevention is achieved with a regular annual early cancer detection examination, with a cytology smear from the portio and colposcopic confirmation if possible.

FORSCHEN
LEHREN
HEILEN

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Prevention and early detection II

6. Diverging from the statutory early detection examination, the following approach can be used:

a) HPV test (Hybrid Capture 2, HC 2) plus conventional cytology with an extended examination interval for women from the age of 30 onward (2–5-year interval).

b) HPV test (HC 2) plus liquid-based cytology with an extended examination interval for women from the age of 30 onward (2–5-year interval).

c) Liquid-based cytology instead of conventional cytology from the age of 20 onward, with a 2-year interval.

d) Computer-assisted cytology.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Patient information I

1. Information materials (print or Internet media) that are of high quality and produced with appropriate specialist competence must be provided, in accordance with the quality requirements set out in the Guideline on Gynecological Information. By communicating the risks in a comprehensible way (including details of incidences, rather than relative percentages), these materials should provide patients with support in taking independent decisions for or against medical procedures.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Patient information II

1 Information should be communicated to the patient both comprehensively and accurately, observing the following basic principles of patient-centered communication:

— Expression of empathy and active listening
— Direct and sensitive ways of touching on difficult subjects
— If possible, avoidance of specialized medical terms, or with explanations of specialist terms being given if necessary
— Strategies for improving understanding (repetition, summing up of important information, use of graphics, etc.)
— Encouraging the patient to ask questions
— Permission and encouragement to express emotions
— Offering further assistance (e.g., from self-help groups, psycho-oncology, psychosocial cancer counseling)

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Diagnosis I

1. Inspection of the portio forms the basis for diagnostic clarification, supplemented in individual cases by colposcopy and bimanual vaginal and rectovaginal examination and colposcopy-guided tissue biopsy of abnormal findings.
2. FIGO staging is carried out during a clinical examination with speculum inspection and bimanual vaginal and rectal examination.
3. If there is an endocervical process, curettage of the uterus is necessary.
4. From FIGO stage IB2 onward, magnetic resonance imaging (MRI) should be used to assess the size of the tumor, its relationship to adjacent organs, and the depth of infiltration.
5. Further imaging diagnosis: chest radiography; transvaginal ultrasonography, ultrasonography of the kidneys bilaterally and of the liver; cystoscopy and rectoscopy.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Diagnosis II

6 Useful diagnostic measures, depending on the stage: multiple biopsies from the vagina; histological assessment of suspicious lymph nodes (cervical and inguinal scalene region); biopsy of infiltrates in the lesser pelvis; laparoscopy or laparotomy to assess locoregional spread.

7 Preoperative laboratory tests: blood count, electrolytes, coagulation, creatinine, transaminases, alkaline phosphatase, gamma-glutamyl transferase, urine status.

8 Laboratory tests that are useful in individual cases: SCC or CEA/CA 12-5 in adenocarcinoma; neuron-specific enolase (NSE) in neuroendocrine carcinomas; creatinine clearance in the presence of hydronephrosis and planned chemotherapy.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Pathology of precancerous lesions

1. Histological classification of precancerous lesions and invasive carcinoma is carried out in accordance with the WHO requirements.
2. The minimum requirements for reporting histopathological findings after conization are: size and composition of the cone specimen; type of lesion (CIN, ACIS); the location of the lesion (endocervical, ectocervical); its extent; and any invasive changes that may be present. It is obligatory to provide firm details concerning the resection margins.

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Pathology of invasive carcinoma

3 Postoperative staging is carried out using the TNM classification.

4 The minimum requirements for reporting histopathological findings in cervical carcinoma are: tumor stage, tumor size, pelvic and para-aortic lymph-node metastases, depth of invasion, grading, histological tumor type, vascular and lymphatic invasion, and R classification.

5 Prognostic factor for microinvasive cervical carcinomas: depth of invasion.

6 Prognostic factors for macroinvasive cervical carcinomas: tumor stage, evidence of lymph-node metastases, tumor size, histological type, grade of differentiation, relative depth of invasion, lymphatic invasion.

FORSCHEN
LEHREN
HEILEN

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Basic principles of treatment

1. In the early stages, and particularly in premenopausal patients, surgery is recommended.
2. In FIGO stages Ib and II, surgery and simultaneous radiotherapy and chemotherapy lead to long-term results that are in principle equivalent, with different recurrence patterns and side effect profiles for the treatments.
3. In FIGO stage III, there is an indication for simultaneous chemoradiotherapy.
4. In FIGO stage IV, the choice of treatment should be made on an individual basis.

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
UTERUS KOMMISSION
© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Surgical techniques: conization

1. Conization should be carried out with an electrosurgical loop, or with laser conization. These techniques are superior to knife conization in terms of side effects.
2. Conization during pregnancy should only be carried out when there is cytological or colposcopic suspicion of invasive carcinoma.
3. The Sturmdorf suture is obsolete.

FORSCHEN
LEHREN
HEILEN

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Surgical techniques: surgical staging

Staging laparoscopy and staging laparotomy may be useful for assessing parametrial and/or vesicouterine spread and for assessing the pelvic and/or para-aortic lymph nodes.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Surgical techniques: radical abdominal operation I

The principle of the operation involves the following steps:

1 Opening of the abdominal cavity and systematic inspection.

2 In premenopausal women, it is possible to preserve the ovaries.

3 Opening of the paravesical fossa. If there is suspected tumor involvement, frozen-section evaluation can be carried out. When there is marked tumor involvement, the operation is stopped or partial bladder resection or exenteration are carried out.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Surgical techniques: radical abdominal operation II

4 Incision into the Douglas peritoneum and opening of the pararectal fossa; removal of connective and fatty tissue with the lymph tracts and nodes medial to the internal and external common iliac vessels, with abrasion of the obturator groove.

5 Mobilization of the rectum and removal of the sacrouterine ligaments.

6 Complete dissection of the uterus out of the parametria.

7 Mobilization of the ureter after dissection of the bladder pillar.

8 Removal of the paracolpium and vagina, depending on the size of the primary tumor and involvement of the vagina.

Surgery for early cervical carcinoma

1 Following an individualized and shared decision-making process, treatment for stage IA1 cervical carcinoma can be carried out using conization in a fertility-preserving fashion, or with hysterectomy.

2 Following an individualized and shared decision-making process, treatment for stage IA1 L1 cervical carcinoma can be carried out using conization or trachelectomy plus pelvic lymphadenectomy in a fertility-preserving fashion, or with hysterectomy plus pelvic lymphadenectomy.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Surgery for cervical carcinoma: special cases

1. Radical vaginal surgery with the Schauta–Amreich procedure: this is an alternative to the abdominal procedure, particularly in tumors < 4 cm, in the absence of lymphatic or vascular involvement, and in G1 and G2 carcinomas.
2. Trachelectomy: prerequisites are G1 and G2 squamous cell carcinomas, an absence of lymphatic or vascular involvement, and a tumor size of less than 2 cm. The resection margin near the uterus should have a safety margin of at least 0.5 cm. The pelvic lymph nodes that are removed must be free of tumor.
3. Primary exenteration: in selected cases, exenteration may also be indicated — for example, to prevent cloacal formation.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Surgery for cervical carcinoma

1. Surgical treatment for stage IA2 and IB1 cervical carcinoma is indicated in the form of radical hysterectomy with systematic pelvic lymphadenectomy.
2. From FIGO stage IB2 to IIB, lymphadenectomy should initially be carried out para-aortically, caudal to the inferior mesenteric artery. If the lymph nodes are involved, complete para-aortic lymphadenectomy should be carried out as far as the renal pedicle. If these upper lymph nodes are also involved, the operation should be stopped.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Chemo-Radiotherapy

1. Primary radiotherapy always consists of a combination of percutaneous therapy and afterloading therapy. Primary radiotherapy must be carried out with simultaneous cisplatin administration. Dosage: 40 mg/m^2 weekly; five cycles should be administered.
2. Adjuvant radiotherapy reduces the risk of local recurrence, but does not improve the survival. There are no advantages for combination chemotherapy in comparison with monotherapy with cisplatin.
3. In the presence of risk factors (positive lymph nodes, tumor size 4 cm, deep stromal invasion, R1 resection, extensive parametrial infiltration, inadequate lymphadenectomy, extensive lymphatic/vascular involvement), adjuvant radiotherapy or chemoradiotherapy should be carried out.
4. In persistent tumors, the decision on whether to carry out secondary hysterectomy or exenteration should be taken on an interdisciplinary basis.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Chemotherapy

1. Neoadjuvant platinum-containing chemotherapy, carried out with short intervals and with an intensified dosage, improves operability and reduces the incidence of positive lymph nodes.
2. There is no evidence of any clinical benefit for adjuvant chemotherapy.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Treatment of CIN lesions

1. In histologically confirmed CIN 1, only regular check-ups should be carried out.
2. In CIN 2 and CIN 3 histologically confirmed by biopsy during pregnancy, only follow-up checks should be carried out.
3. In CIN 2 and CIN 3 lesions that persist for more than 12 months outside pregnancy, surgery is indicated.

ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Supportive therapy

1 Supportive treatment in accordance with the guidelines for prevention and minimization of treatment-related or tumor-related symptoms is required.

FORSCHEN
LEHREN
HEILEN

ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

FORSCHEN
LEHREN
HEILEN

Psycho-oncology

1. Psycho-oncological care for patients with cervical carcinoma forms an integral part of oncological diagnosis, treatment, rehabilitation and follow-up and represents an interdisciplinary task.
2. The patient should receive information at an early stage regarding the availability of in-patient and outpatient psycho-oncological support and skilled psycho-oncological care if needed.
3. The patient's quality of life should be regularly assessed during treatment, rehabilitation and follow-up, also in order to assess the potential need for psycho-oncological support.

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Rehabilitation

1. All patients should be informed and advised in detail by the attending physician regarding the statutory facilities for subsequent treatment, regular therapy, and outpatient rehabilitation.

FORSCHEN
LEHREN
HEILEN

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Follow-up I

1. Aspects requiring attention during the follow-up include: genital atrophy phenomena (dyspareunia), lymphedema in the lower extremities, radiogenic reactions in the ureter, bladder, and bowel, and hormonal deficiencies.
2. Since a curative approach is possible if a local recurrence is recognized at an early stage, a 3-month follow-up interval should be observed in the first 2–3 years after primary therapy, with speculum examination, vaginal and rectal examination, and ultrasonography if appropriate.

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Follow-up II

3 More detailed imaging diagnosis is only required in symptomatic patients.

4 The following points should be addressed in discussion with the patient during the follow-up:

— Transient and long-term effects of the disease and treatment

— Assistance available (self-help groups, psychosocial cancer counseling services)

— Psycho-oncological/psychotherapeutic treatment facilities

— Sexuality and relationship

— Quality of life

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Recurrence/metastases I

1. Central recurrence: if there are no signs of distant metastases, then depending on the location, anterior exenteration (if the bladder is involved), posterior exenteration (if the rectum is involved), or complete exenteration are possible.
2. Pelvic wall recurrence: if only surgical treatment has previously been carried out, simultaneous chemoradiotherapy. If chemoradiotherapy has already taken place, special surgical procedures are possible in individual cases (e.g., laterally extended endopelvic resection, LEER), if appropriate in combination with interstitial radiotherapy (intraoperative radiotherapy, IORT). These procedures are experimental.

Recurrence/metastases II

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

3 Para-aortic metastases: if there are isolated para-aortic lymph-node metastases, surgical removal of them is useful in individual cases. This is indicated if no radiotherapy or chemoradiotherapy has previously been carried out.

4 Deep vaginal recurrence: colpectomy is useful if technically feasible, or chemoradiotherapy with a second caudal irradiation field is possible if technically feasible.

Recurrence/metastases III

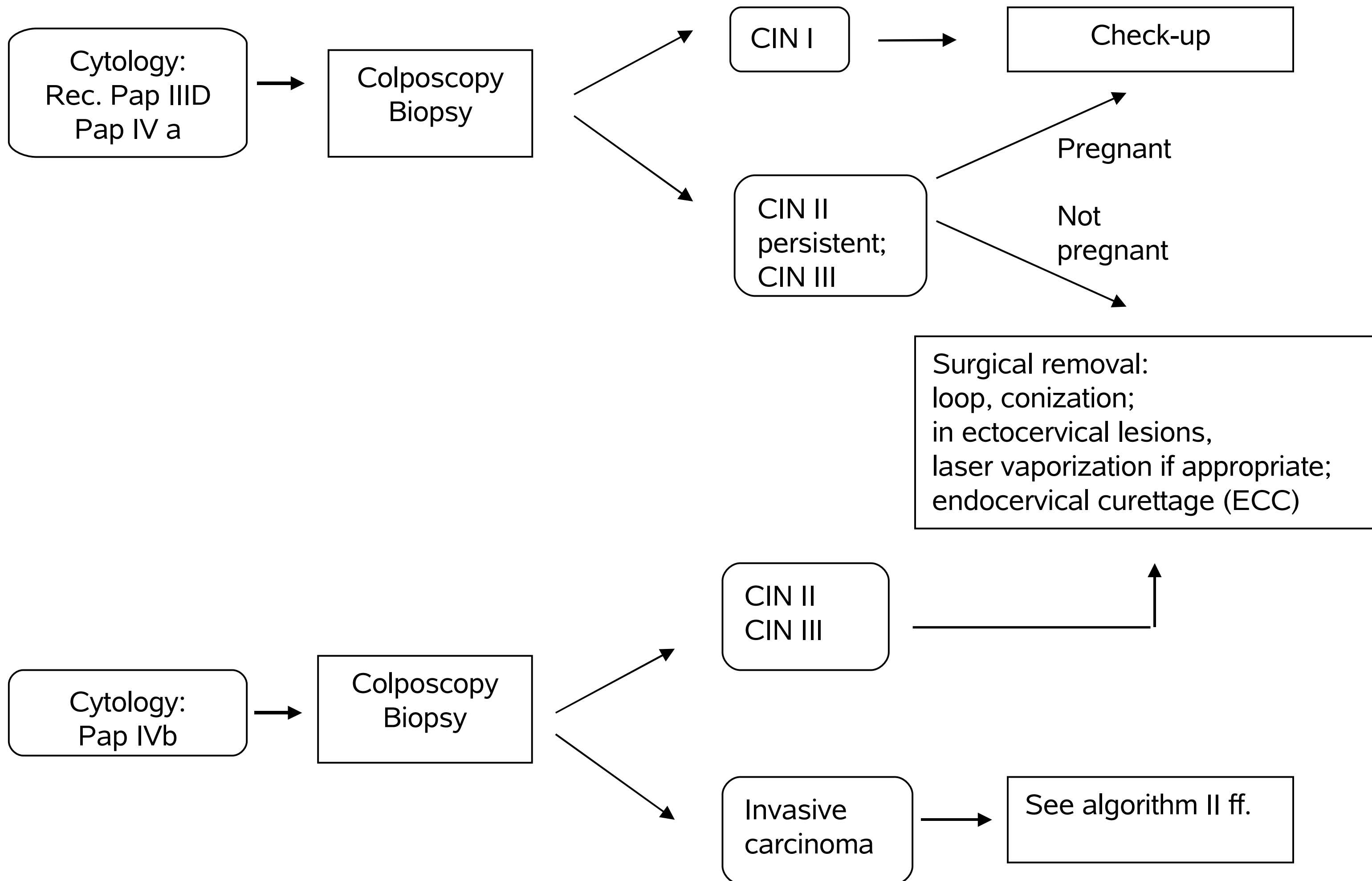
© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

5 Palliative chemotherapy:

If surgery or chemo(radio)therapy for a recurrence or metastases is not possible, palliative chemotherapy must be considered.

In the case of local recurrences in the lesser pelvis and status post radiotherapy or chemoradiotherapy, the response rate to chemotherapy is low. The improvement in the median survival is less than 6 months. The best results are achieved with combinations of cisplatin with paclitaxel and cisplatin with topotecan.

Algorithm: treatment of preinvasive lesions



AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
UTERUS KOMMISSION
© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

FORSCHEN
LEHREN
HEILEN

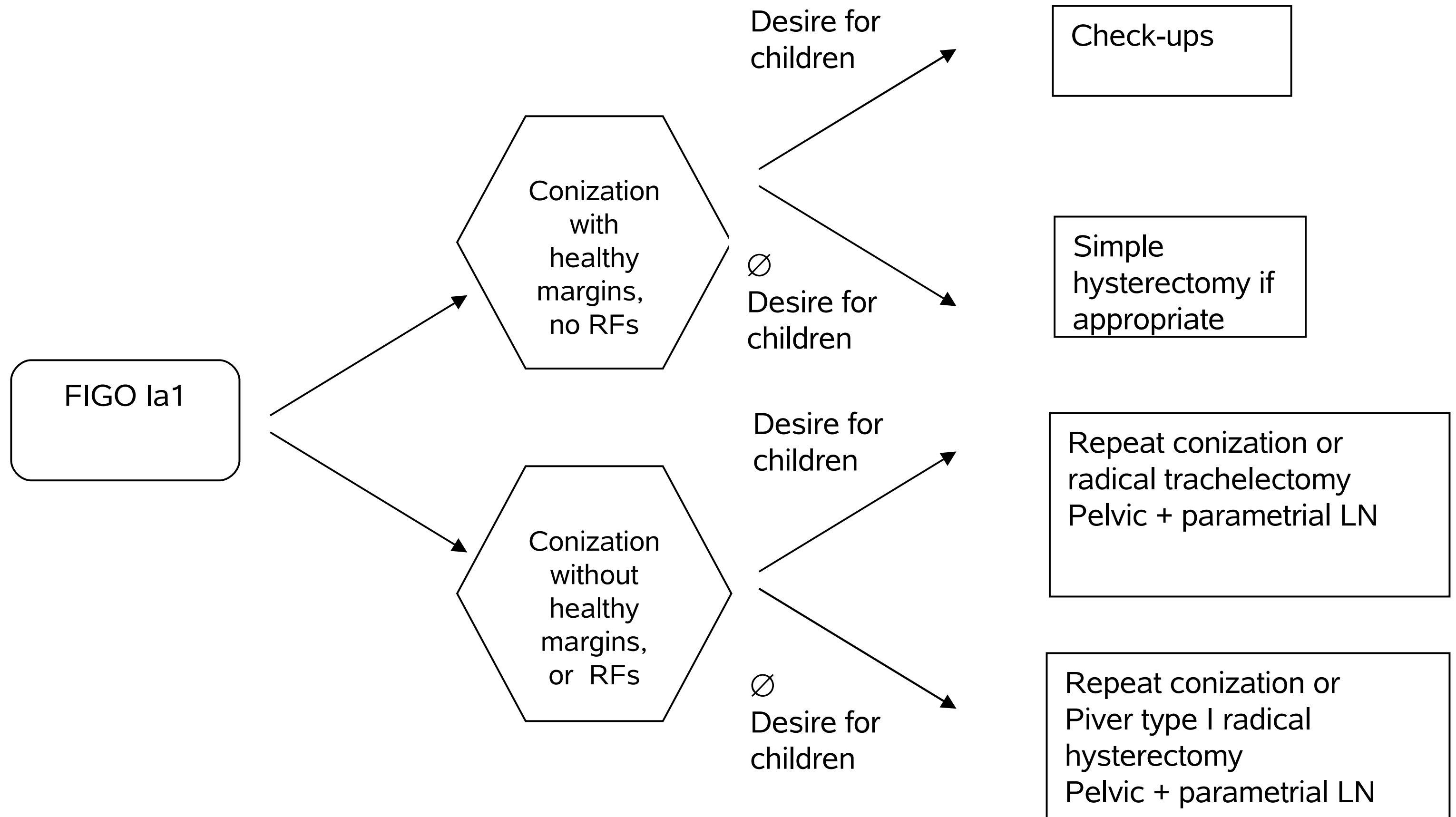
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Algorithm: stage Ia



RF: Risk faktors
LN: Lymphadenectomy

FORSCHEN
LEHREN
HEILEN

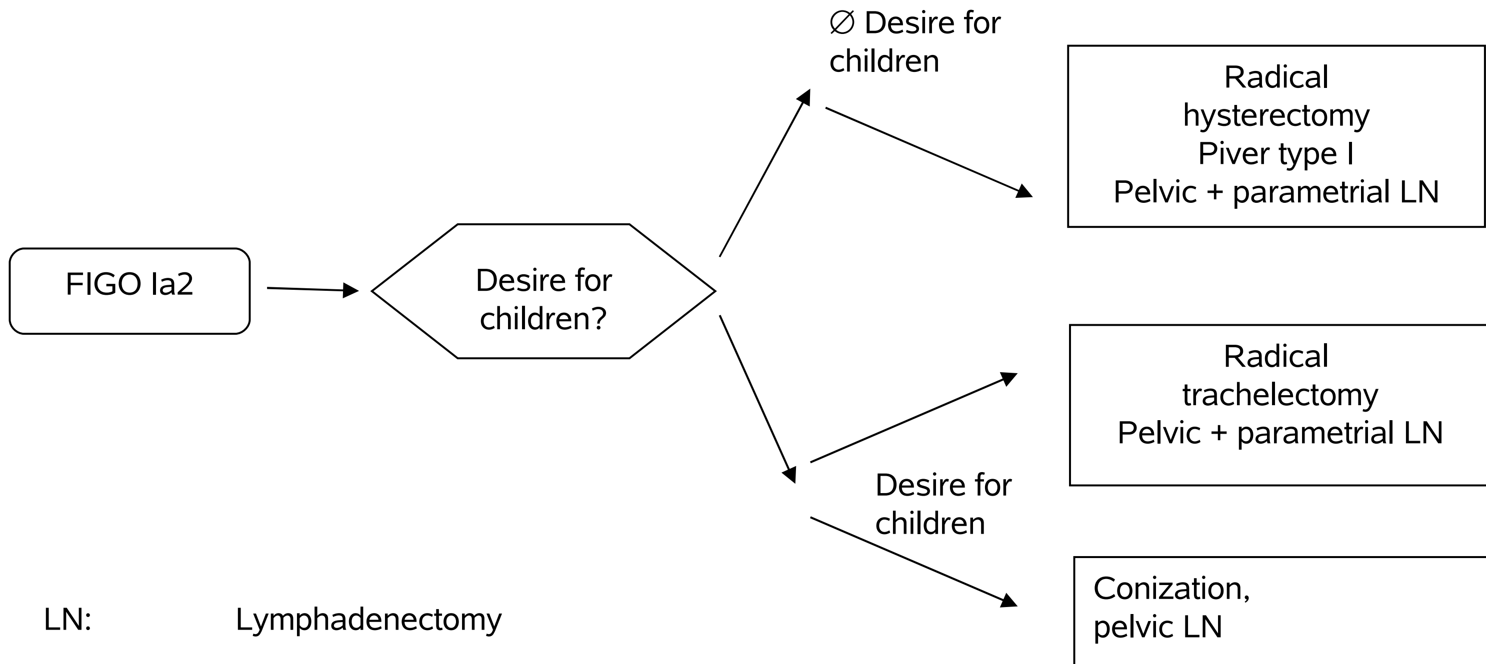
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Algorithm: stage Ia

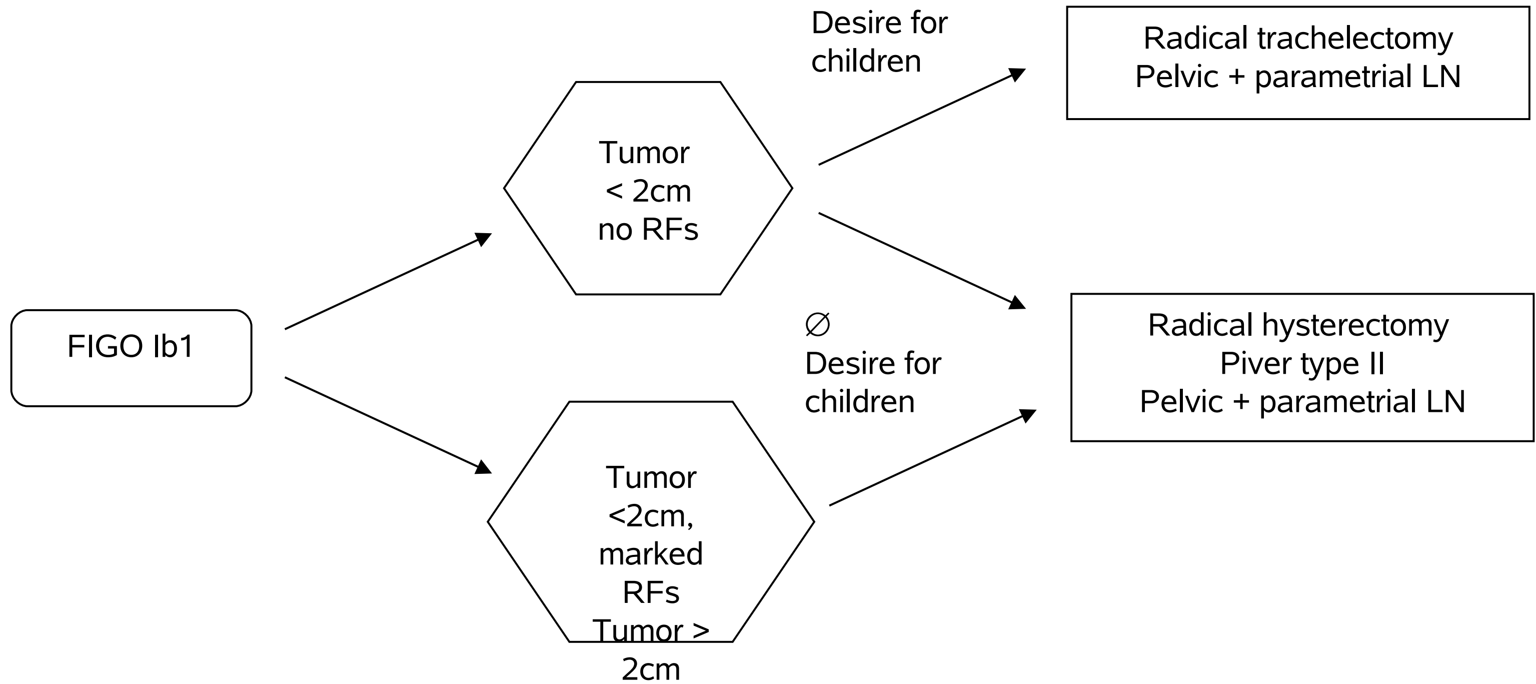


FORSCHEN
LEHREN
HEILEN

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

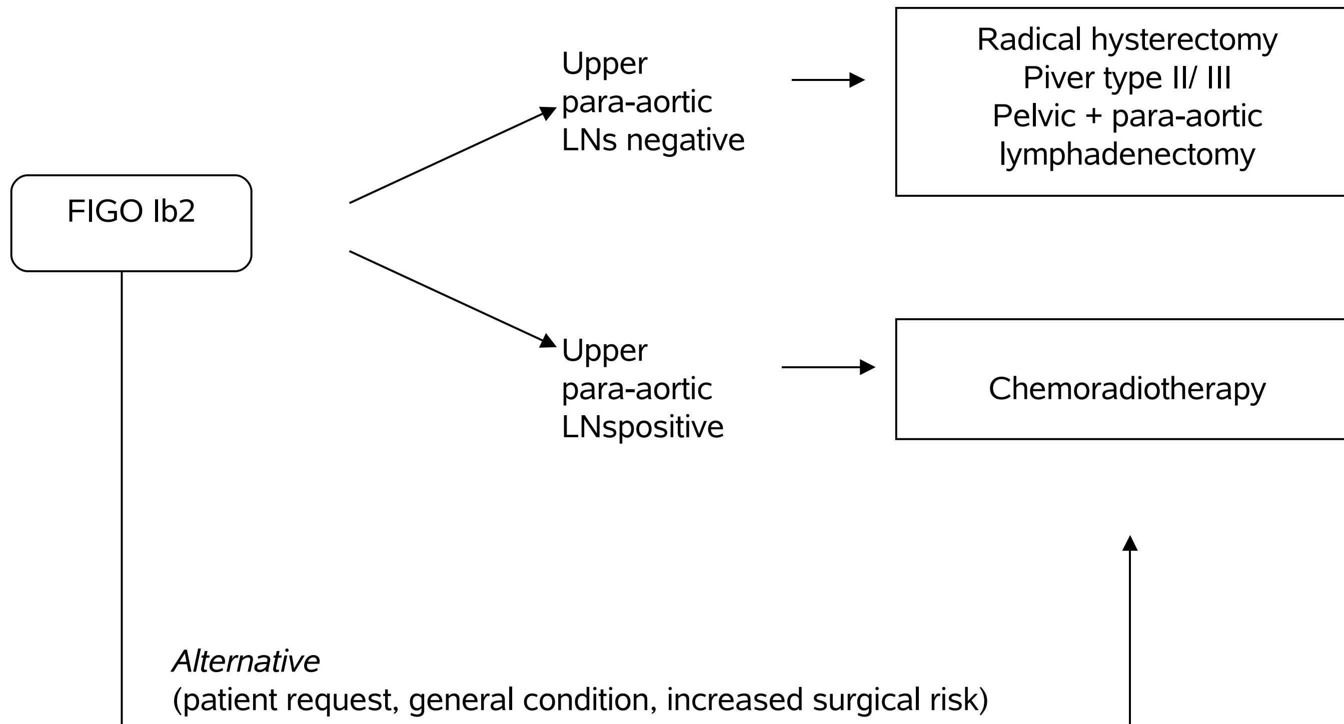
Algorithm: stage Ib



RF: Risk factors (lymphatic or vascular involvement, G3)
LN: Lymphadenectomy

AGO ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
UTERUS KOMMISSION
© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Algorithm: stage Ib

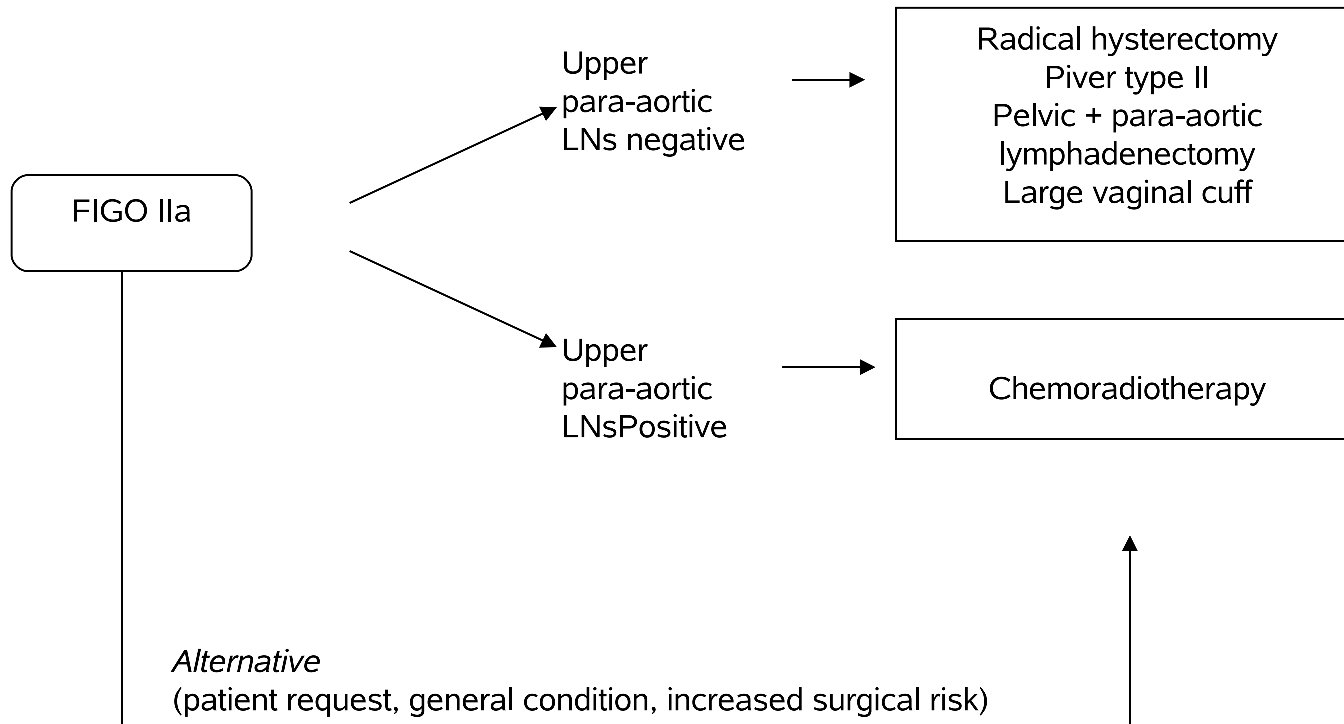


FORSCHEN
LEHREN
HEILEN

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
UTERUS KOMMISSION
© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

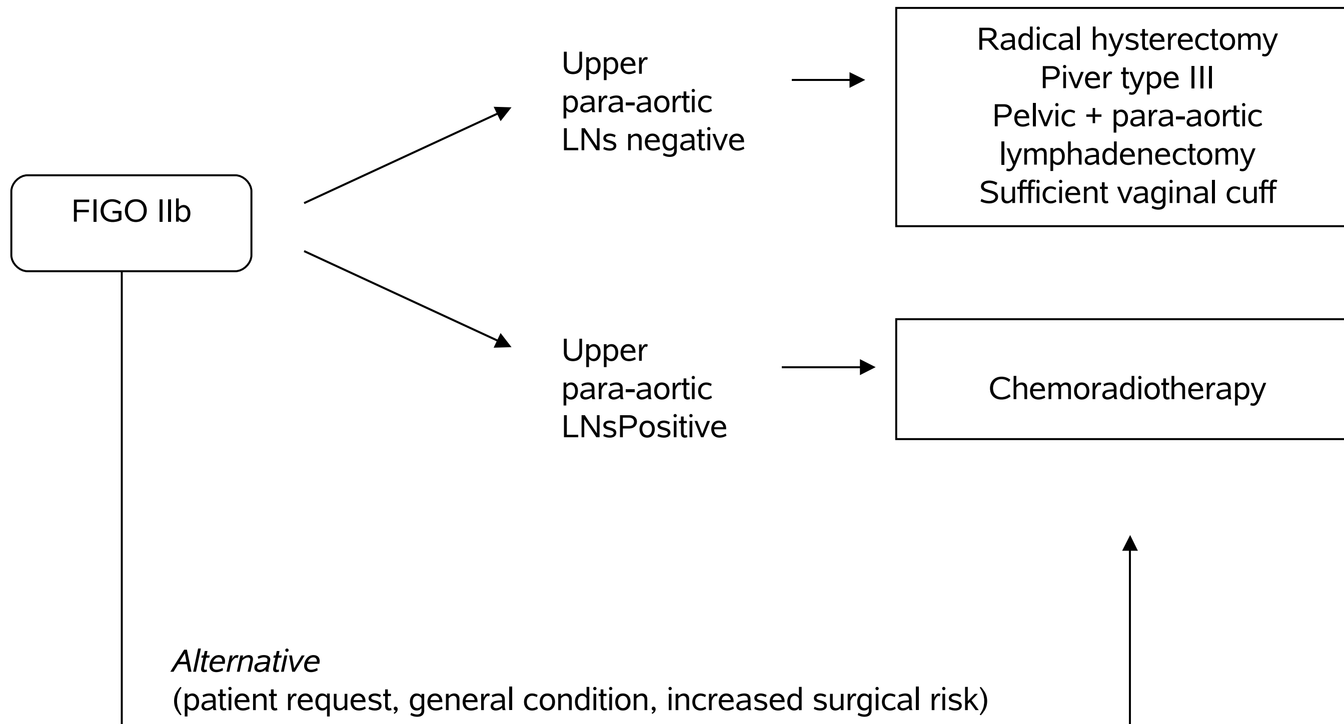
S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Algorithm: stage IIa



FORSCHEN
LEHREN
HEILEN

Algorithm: stage IIb



© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

FORSCHEN
LEHREN
HEILEN

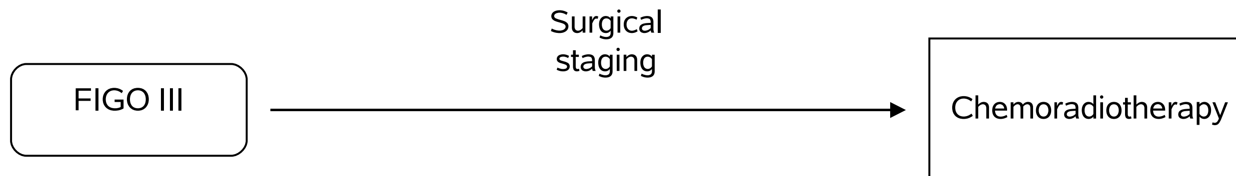
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.

UTERUS KOMMISSION

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

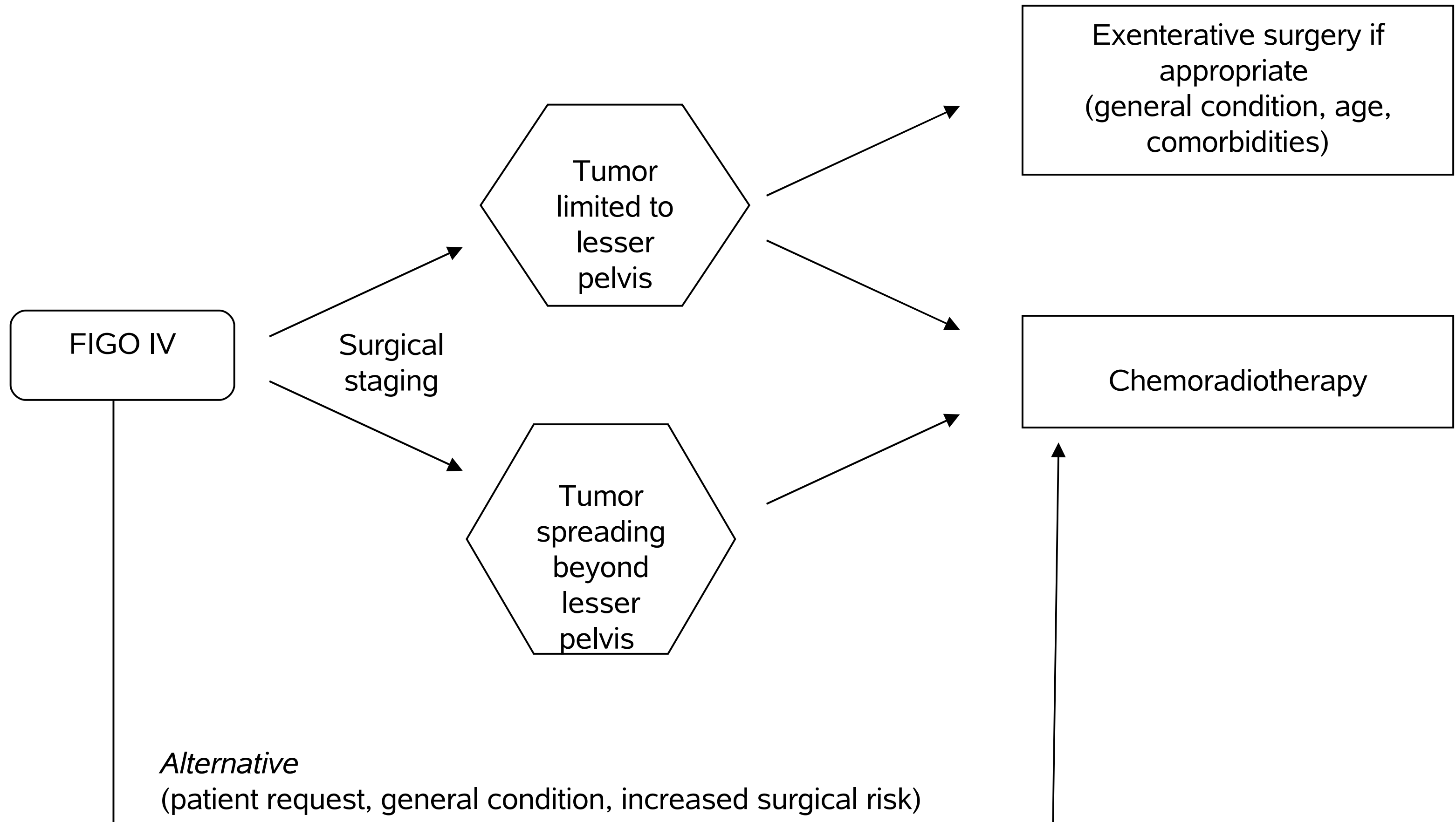
S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

Algorithm: stage III



FORSCHEN
LEHREN
HEILEN

Algorithm: stage IV



© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

S2k Cervical Carcinoma Guideline
Version 2.0
1 February 2008

FORSCHEN
LEHREN
HEILEN