Thieme

Standardized Procedures for Patients with Dysplasia and Other Diseases of the Cervix, Vulva, and Vagina at a Certified Dysplasia Unit Prior to the Introduction of the Organized Cervical Cancer Screening Program

Standardisierte Abläufe für Patientinnen mit Dysplasien oder Erkrankungen der Zervix, Vulva und Vagina an einer zertifizierten Dysplasie-Einheit vor Einführung des organisierten Zervixkarzinom-Früherkennungsprogramms

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Schlüsselwörter

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ABSTRACT

Introduction Gynecologic dysplasia units and dysplasia consultations are obliged to offer diagnosis and treatment in accordance with the guidelines. The organization of the consultation process, management of patient appointments, diagnosis, and treatment algorithms are heterogeneous. The legislation arising from the new Federal Joint Committee decision, dated 22 November 2018, concerning the organized cervical cancer screening program has been in force since 1 January 2020. In this article we provide an overview of the existing structures and interdisciplinary cooperation of specialized dysplasia units incorporated in certified gynecologic cancer center.

Materials and Methods We carried out a retrospective database search of data collected prospectively from 1 July 2014 to 31 December 2019 at the dysplasia unit at the Department of Gynecology and Obstetrics, Erlangen University Hospital, which was the first dysplasia unit to be certified in 2014.

Results A total of 5594 patients presented at the unit, and 16 061 colposcopic, vulvoscopic, and anoscopic examinations were performed. Approximately 4100 examinations of the cervix, vagina, vulva, and anus are carried out each year, 1600 of these were exclusively cervix colposcopies. A total of 12 197 cytology results were assessed, as well as 4850 histology results, and 8193 high-risk HPV tests. The quality indicators required by the dysplasia unit for annual recertification were met each year.

Conclusion Certified dysplasia units and consultations form the central component in the algorithm for further investigating abnormal screening results; but they are also the first point of contact for a large number of patients with acute or chronic complaints in the genital region.

ZUSAMMENFASSUNG

Einleitung Gynäkologische Dysplasie-Einheiten und Dysplasie-Sprechstunden sind verpflichtet, leitliniengerechte Diagnostik und Therapie anzubieten. Der organisatorische Ablauf der Sprechstunde, das Einbestellmanagement, die Diagnose und Therapiealgorithmen sind heterogen. Das Gesetz des neuen G-BA-Beschlusses vom 22.11.2018 über das organisierte Programm zur Früherkennung des Zervixkarzinoms ist seit 01.01.2020 aktiv. Diese Arbeit gibt einen Überblick über die vorhandenen Strukturen sowie die interdisziplinäre Zusammenarbeit einer spezialisierten Dysplasie-Einheit eingebettet in ein zertifiziertes Gynäkologisches Krebszentrum.

Material und Methoden Es erfolgte eine retrospektive Datenbankabfrage prospektiv erhobener Daten in der 2014 erstzertifizierten Dysplasie-Einheit der Erlanger Frauenklinik vom 01.07.2014 bis 31.12.2019.

Ergebnisse Insgesamt stellten sich 5594 Patientinnen vor; es erfolgten 16 061 kolposkopische, vulvoskopische und anoskopische Untersuchungen. Es finden jährlich circa 4100 Kolposkopien der Zervix, Vagina, Vulva und des Anus statt, davon 1600 alleinige Zervix-Kolposkopien. Insgesamt wurden 12 197 zytologische Ergebnisse sowie 4850 Histologien und 8193 High-Risk-HPV-Testungen ausgewertet. Die Qualitätsindikatoren, die jährlich für die Zertifizierung einer Dysplasie-Einheit erforderlich sind, wurden jährlich erreicht.

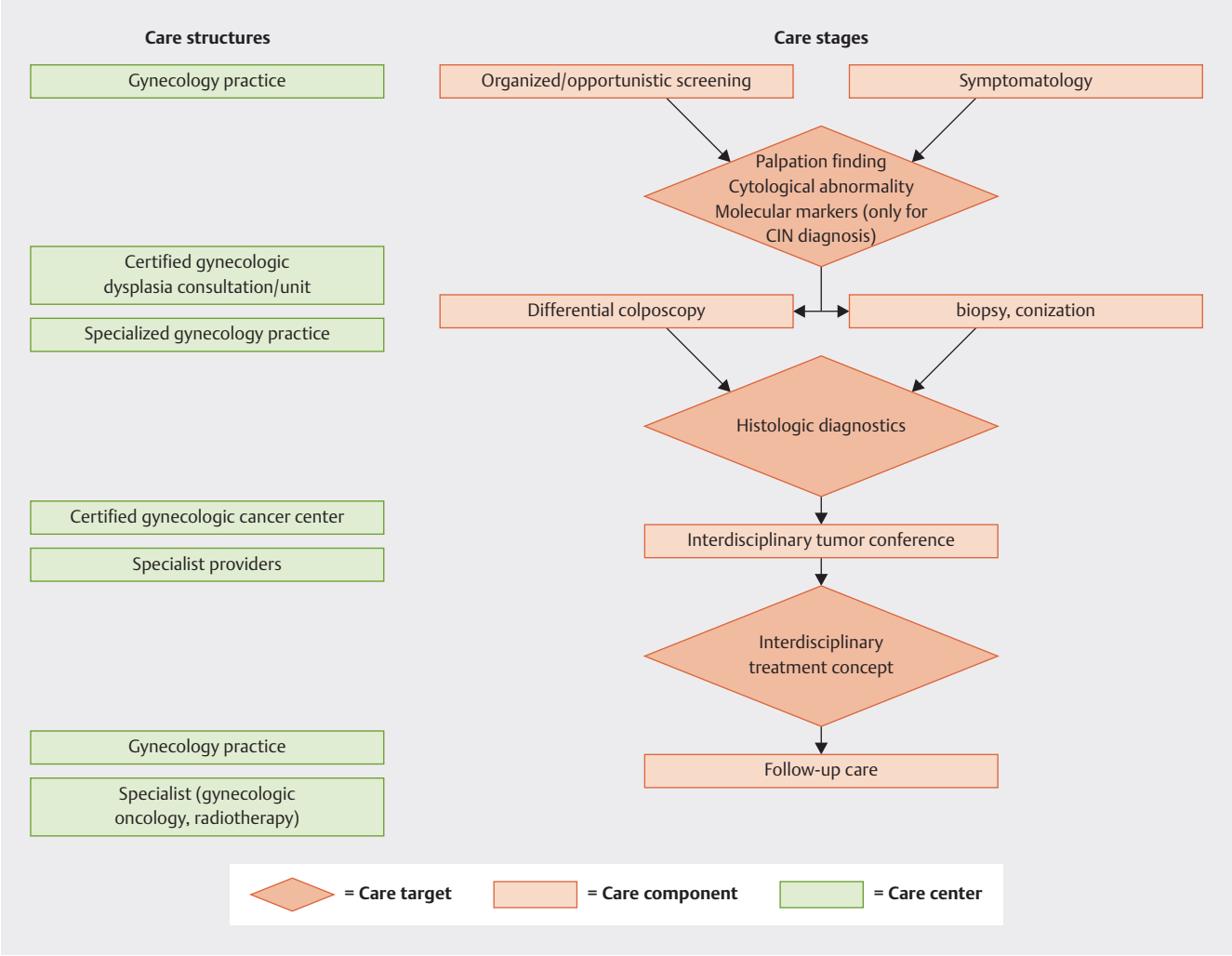
Schlussfolgerung Zertifizierte Dysplasie-Einheiten und -Sprechstunden sind der zentrale Baustein im Abklärungsalgorithmus von auffälligen Screeningbefunden, zusätzlich aber auch Anlaufstelle für eine Vielzahl von akuten oder chronischen Beschwerden im Genitalbereich.

Introduction

In Germany there are currently 168 gynecologic cancer centers that are certified by the German Cancer Society (DKG) (as of March 2022) [1]. In Germany and German-speaking regions there are 36 certified dysplasia units and 191 certified dysplasia consultations (as of November 2020) [2].

The division into a dual certification system can be explained based on the different requirement profiles: dysplasia consultations are tied to individuals, and in the context of certification they are subject to less extensive requirements. Certification is granted based on documentation evaluated by the Working Group for Cervical Pathology and Colposcopy e. V. (in German: AG-CPC). Coordination, publication, and archiving of certifications is then managed by OnkoZert, an independent institute responsible for the certification process. Gynecologic dysplasia units are tied to individuals and institutions. Compared to dysplasia consultations, they are required to meet a higher standard of medical expertise, advanced training and education, and research. The certification is administered by OnkoZert in a three-year cycle. It is based on the fulfillment of medical requirements and characteristics described in the questionnaires and KPI forms (KPI: key performance indicator), and is subject to an on-site audit by medical specialists in which the structures and processes of the dysplasia unit are reviewed. In addition, annual KPIs must be submitted as specific, quantifiable elements for assessing the quality of results. These KPIs include inter alia attendance of an interdisciplinary tumor conference, indication for surgery in cases of CIN II+, and information on postoperative resection status. These benchmarks are then published in the individual and combined annual reports [3].

The consented care algorithm of the interdisciplinary care chain for cervical cancer patients is illustrated in ▶ **Fig. 1** [4, 5]. If any abnormalities are detected in gynecology examinations, the patient is referred to a dysplasia unit or dysplasia consultation for further diagnostics. This unit is affiliated to a gynecologic cancer center (in German: GKZ) certified by the DKG. Dysplasia units may be linked to additional dysplasia consultations. In the diagnostic process, the interdisciplinary tumor meeting serves as a central decision-making body for all carcinomata, as well as for difficult or rare cases of dysplasia. The GKZ collaborates closely with its inter-



▶ **Fig. 1** Approved algorithm for patients with cervical cancer [4].

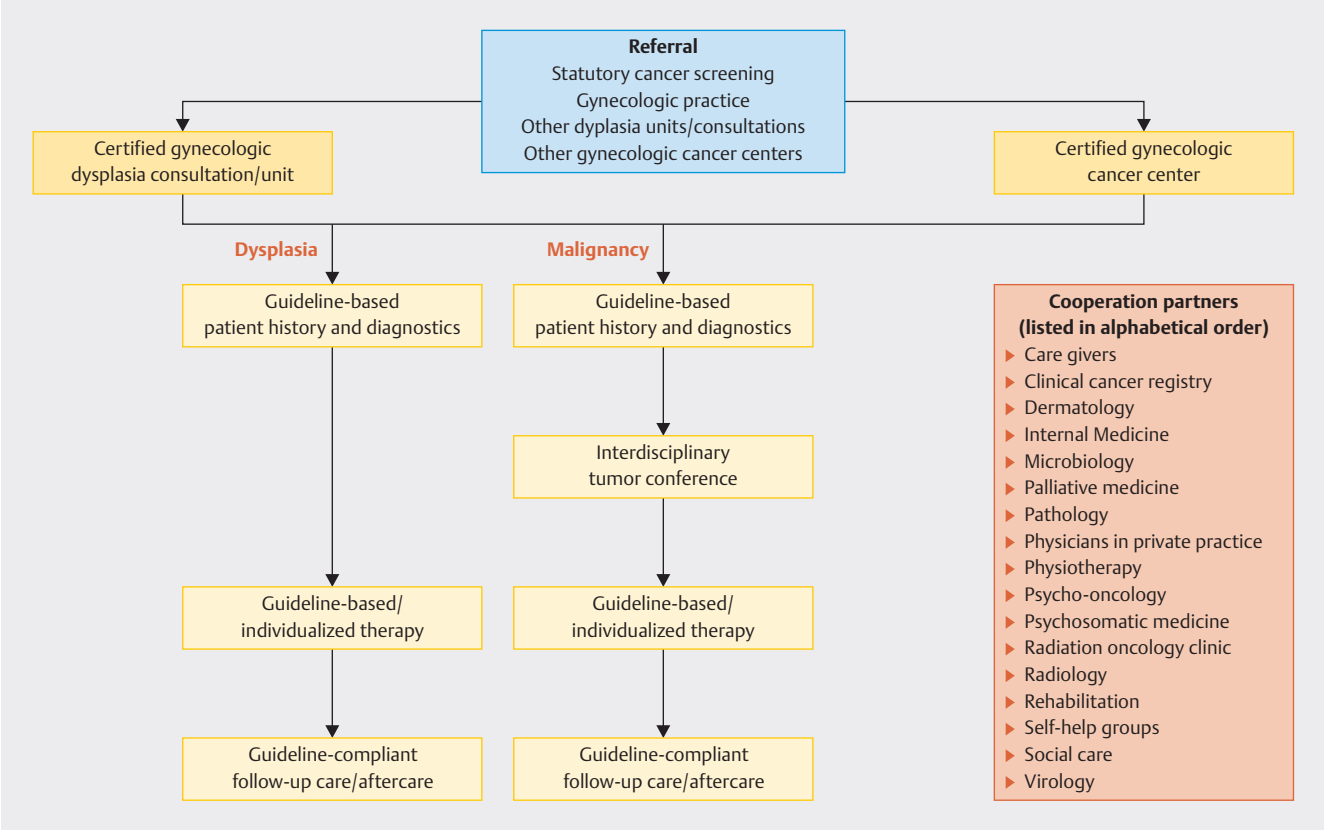
disciplinary cooperation partners. The pathways for patients with malignancies and dysplasia are set out in ▶ **Fig. 2**.

These structural elements provide a basis for investigating abnormal findings detected in the context of opportunistic cervical screening, and for switch to an organized, HPV-based cervical cancer screening program.

Scientific investigations of the dysplasia unit have been published on individual prognosis factors such as tumor budding in the development of squamous epithelial cervical carcinoma, HPV integration and subtyping, the consistency of external vs. in-house cytologic results, of colposcopic or vulvoscopic impressions and histology performed, and the accuracy of biopsies of the cervix, vulva and vagina performed by colposcopy [6, 7, 8, 9, 10, 11, 12]. This research has been presented at various scientific conferences.

For clinical, professional, and scientific reasons, the director of the dysplasia unit is distinguished as an AG-CPC trainer and member of the Vulva Vagina Committee of the Working Group for Gynecologic Oncology (AGO). Colposcopy training courses with examinations leading to the colposcopy diploma are offered annually (basic and advanced courses according to the curriculum of the AG-CPC). External observation placements in this area are also regularly offered. In addition, a clinical colposcopic cytology and histology conference is held quarterly, via the Comprehensive Cancer Center Erlangen/European Metropolitan Region Nuremberg (CCC ER-EMN), as a forum to discuss cases from the dysplasia unit and the GKZ involving clinical examination, cytology, histology and pathology of biopsies, and/or surgery using digital cytology and pathology. A quarterly quality circle also takes place. All treating physicians are members of the AG-CPC, and have obtained the colposcopy diploma.

In this article we present a retrospective analysis of the structures of the dysplasia unit in the Women's Hospital of the University Hospital Erlangen, the first unit to be certified in Germany, prior to the introduction of the cervical cancer screening program which has been in place since 1 January 2020 [13]. The certified dysplasia unit and colposcopy consultation represents a central point of contact for patients with cytology abnormalities, persistent HPV infection, and a large variety of other genital diseases. The aim of this article is to present the standardized procedures that have been established in our certified dysplasia unit.



▶ **Fig. 2** Procedures at the Gynecologic Cancer Center of Franconia for collaboration with the dysplasia consultations/dysplasia units and additional cooperation partners; pathways for patients with malignancies and dysplasia.

Methods

The dysplasia consultation at the Women's Hospital of the University Hospital Erlangen was first certified in May 2014 (Dys-E001) as a dysplasia unit in cooperation with the University Gynecologic Cancer Center of Franconia. Certification was administered in accordance with the criteria of the DKG, the German Society for Gynecology and Obstetrics e.V. (DGGG), the working group for gynecologic oncology (AGO), and the AG-CPC.

The cytology results are evaluated according to Munich Nomenclature III [14, 15]. Following the conversion from Munich Nomenclature II to the new Munich Nomenclature III which took effect on 1 July 2014, 2351 cytology smears were not included in this evaluation, because they were taken during the transition phase and could not be adequately converted into the new Munich Nomenclature III.

Patient Cohort

During the period from 1 July 2014 to 31 December 2019, 5594 patients attended 9772 appointments in our dysplasia unit. The subcohorts are not congruent because the diagnostics (cytology, colposcopy, HPV and histology) performed at each individual presentation were not identical for all patients. The same applies for the surgeries included in our analysis, as only a subsection of the total cohort underwent surgery depending on the indication.

Due to spatial and structural overlaps with the GKZ in patients with urgently suspected or confirmed carcinoma of the cervix, vagina, or vulva, these patients were excluded from the surgical cohort based on the objective of this study to present solely the dysplasia unit. Moreover, the histologic, cytologic, and colposcopic findings only represent a portion of the invasive cancers since externally confirmed diagnoses were captured via the GKZ, and not via the dysplasia unit.

Structured Processes

All patients with abnormal Pap smears are primarily examined in the dysplasia unit. Consultation hours are held twice a week. There is a capacity for 20 to 30 patients per consultation. In addition, we have cooperation agreements with practices of three gynaecologists offering dysplasia consultations (as of 2019). In case of abnormalities in the routine examination by gynecologists in private practice, the patient is referred to a certified gynecologic dysplasia consultation or dysplasia unit for further diagnostics and appropriate treatment [16].

The main reasons for referral are abnormal Pap smears detected through the statutory cancer screening program, suspicious lesions, treatment-resistant complaints, or incidental findings detected in other special consultations at the Department of Gynecology and Obstetrics.

▶**Table 1** Comparison of requirements regarding appointment management in dysplasia units.

Cytology finding	OnkoZert requirements (as of July 2020) [17]	In-house standard (up until 31 December 2019)	oKFE-RL (valid from 1 January 2020) [16]
Cancer suspicion or group IVb	Colposcopy appointment < 4 weeks	Max. 2 weeks	Immediately
For cytology group IVa	Colposcopy appointment < 3 months	Max. 4 weeks	Immediately
If pregnant and for cytology group IVa or higher	Colposcopy appointment < 4 weeks	Max. 2–3 weeks	
If pregnant and for cytology group IIID1 to up to the 12 th week of pregnancy (WOP)	Colposcopy appointment up to the 20 th week of pregnancy	Colposcopy appointment up to the 20 th week of pregnancy	

Abbreviations: HPV = human papillomavirus; oKFE-RL = Federal Joint Committee guideline on organized cancer screening programs; UKF ER = Women's Hospital at the University Hospital Erlangen

Management of appointments

During the consultation, and depending on the findings, a central appointment management system ensures that appointments are scheduled in a timely manner. The OnkoZert requirements, as well as the requirements of the cervical cancer screening program set out in the guideline on implementation of the organized cancer screening program (oKFE-RL), are listed in ▶ **Table 1** [17, 18]. Appointments are managed based on the probability of a patient having dysplasia or carcinoma. The OnkoZert requirements regarding appointment management were met.

Medical consultation

Patients are asked to submit their previous findings in advance, or at the latest at the time of their appointment. On the day of the examination, the patient is given a medical history form to fill in their general medical and gynecological history. In addition, as part of the administrative procedure for admission to the outpatient clinic, the patient is given the "Information for patients with suspicious findings in the special outpatient clinic for dysplasia and colposcopy – Certified Gynecologic Dysplasia Unit". This leaflet provides information on how the examination is conducted, which behavioral measures are necessary after a biopsy, and when and how the results will be communicated to them (**supplementary online material: Supplement 1**). In a consultation a symptom-related medical history is taken regarding symptoms, risk factors (e.g., nicotine, sexual behavior), HPV vaccination, desire to have children, previous treatment, and secondary diagnoses of particular relevance (such as immunosuppressive diseases or malignancies).

Clinical examination

Initially, the portio vaginalis uteri is adjusted appropriately using a transparent, single-use speculum (available in four sizes). The area is then dabbed to remove mucus or detritus, and a native smear is taken, as well as a microbiology smear if applicable. After this, separate Pap smears are taken from the portio vaginalis uteri and from the cervical canal (with a swab or cytobrush). Then the HPV smear is taken. Testing in the laboratory was originally performed with the Hybrid Capture 2 High-Risk HPV DNA Test (Qiagen, Düsseldorf) which does not differentiate between HPV subtypes; this was switched to the Abbott RealTime High-Risk HPV Test 2000 (Abbott Laboratories, Chicago, USA) in September 2017. This test detects HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.

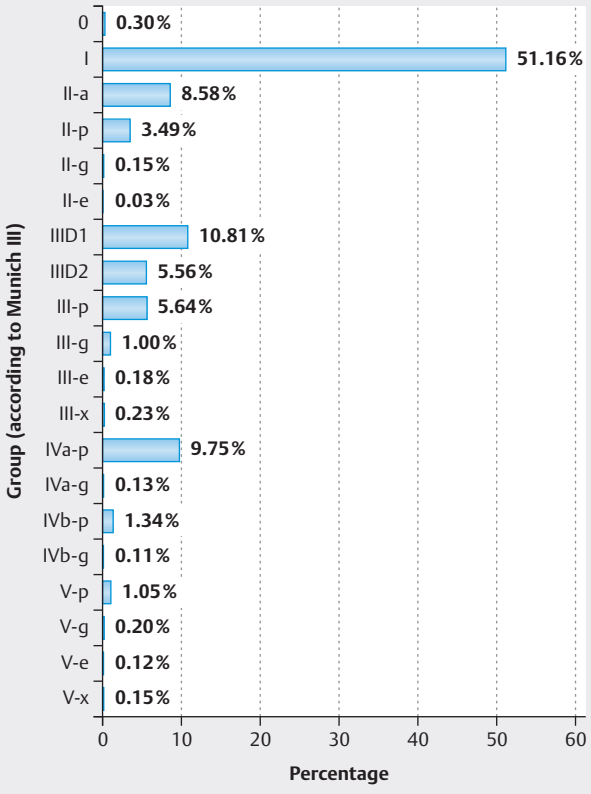
This is followed by differential colposcopy with application of 5% acetic acid solution, Lugol's solution where applicable, green filtering where applicable in the case of suspicious findings (before and after acetic acid), (cervical) strip biopsy, and/or endocervical curettage (ECC), and colposcopic assessment of the vaginal wall, vulva, and anus. Photo or video documentation is recorded using a binocular video colposcope (Zeiss Colposcope KSK 150 FC). A bimanual rectovaginal examination can then be performed as an option depending on the clinical findings. Upon desire, patients can watch the entire examination on a monitor and have abnormalities explained to them. The medical history, examination, photo documentation, and colposcopy results (i.e., suspicion of CIN I–III) is saved as a paperless digital file, and is also added to a database of findings (Microsoft Access). In addition, a sketch of the examination results is documented on paper.

Debriefing

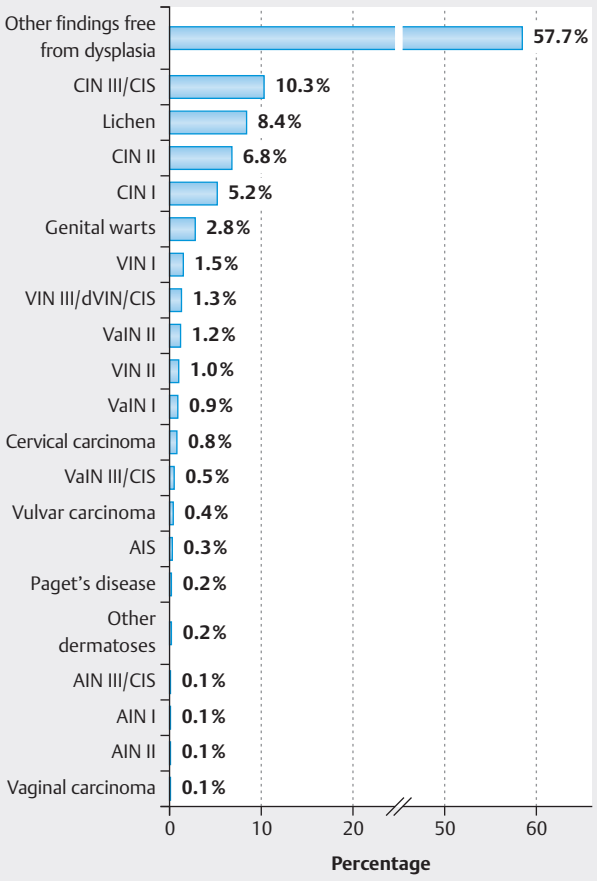
The colposcopic impression of the examination is then discussed with the patient. If surgery is indicated, the lesion and the procedure are explained to the patient with reference to a sketch of the genital region specifically generated by an anatomical draftsman (**supplementary online material: Supplement 2**). After receiving the findings (Pap, HPV, where applicable microbiology smear, histology, etc.), the final diagnosis is made and treatment is commenced as indicated by the specialist/senior physician. Standards for diagnosis and therapy ("Standard Operating Procedure", SOP) exist for common findings, which, if available, are based on the applicable guidelines (**supplementary online material: Supplement 3**). Finally, a doctor's report is sent to the patient and to their gynecologist/referring doctor in private practice.

Interdisciplinary concept

Cases of carcinoma and suspicious findings in post-carcinoma patients detected in the certified gynecological cancer center (in the case of malignancy or unusual disease courses) are presented at an interdisciplinary tumor conference. This involves a close col-



▶ **Fig. 3** Cytology results.



▶ **Fig. 4** Colposcopy results. AIS = adenocarcinoma in situ; CIS = carcinoma in situ; dVIN = differentiated vulvar intraepithelial neoplasia; VIN = vulvar intraepithelial neoplasia

laboration between all cooperation partners (▶ **Fig. 2**). In the dermatological department, a separate interdisciplinary inflammation board is held, in which multimodal therapy options are discussed, for example in the case of dermatological autoimmune diseases.

Statistical Analysis

The cohorts (cytology, HPV, colposcopy, and histology) were constituted from the prospective database of findings, and the type of surgery based on ICD codes and OPS codes for the cervix, vagina, or vulva from the Meierhofer MCC software (**supplementary online material: Supplement 4**) [19, 20, 21, 22]. The exact cohorts were compiled using Microsoft Access 2016 and an SQL (Structured Query Language) script. Descriptive analyses were performed in IBM SPSS Statistics on the distributions and frequencies.

Results

In total, 99.48% of all patients with abnormal Pap smears presenting at the Department of Gynecology and Obstetrics, Erlangen University Hospital, were initially examined in the dysplasia unit.

Diagnostic results

A total of 16061 colposcopic, vulvoscopic, and/or anoscopic examinations were documented. Cytology testing (in accordance with Munich III) was performed in 12197 patients, HPV testing in 8193 patients, and a biopsy was taken in 4850 patients.

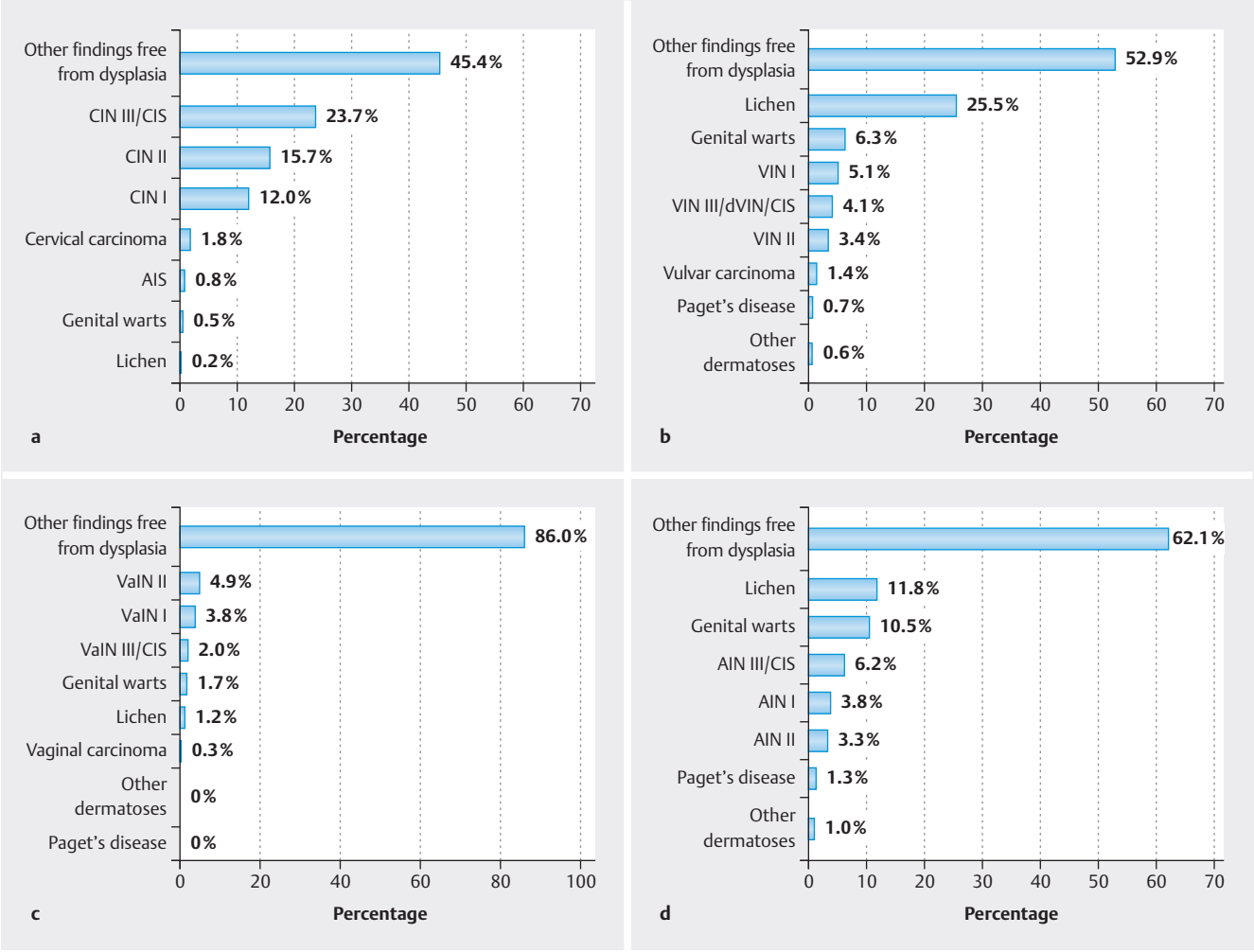
Cytology/HPV

The results of the cytology examinations (n = 12197) are listed in ▶ **Fig. 3**. In 51.2% of patients, the cytology findings were normal (group I). With regard to abnormal cytology findings requiring further diagnostics to confirm dysplasia, 10.8% were in group IIID1, 5.6% in group IIID2, and 9.75% in group IVa-p. Group IVb-p/V findings indicating suspected carcinoma were observed in 2.97% of all cases.

A total of 8193 HPV high-risk tests were documented; among these, 3454 cases (42.2%) were positive and 4739 cases (57.8%) were negative.

Colposcopy

Results from colposcopy/vulvoscopy, and anoscopy obtained immediately after the examination (n = 16061) are presented in ▶ **Fig. 4**. The 16061 examinations of the cervix and/or vulva and/or vagina and/or anus were performed in 5593 patients at 9754



▶ **Fig. 5** Colposcopy results by localization. Cervix (**a**), vulva (**b**), vagina (**c**) or anus (**d**).

appointments. This computes to around 1.7 appointments per patient and 2.9 colposcopies per patient for the period analyzed.

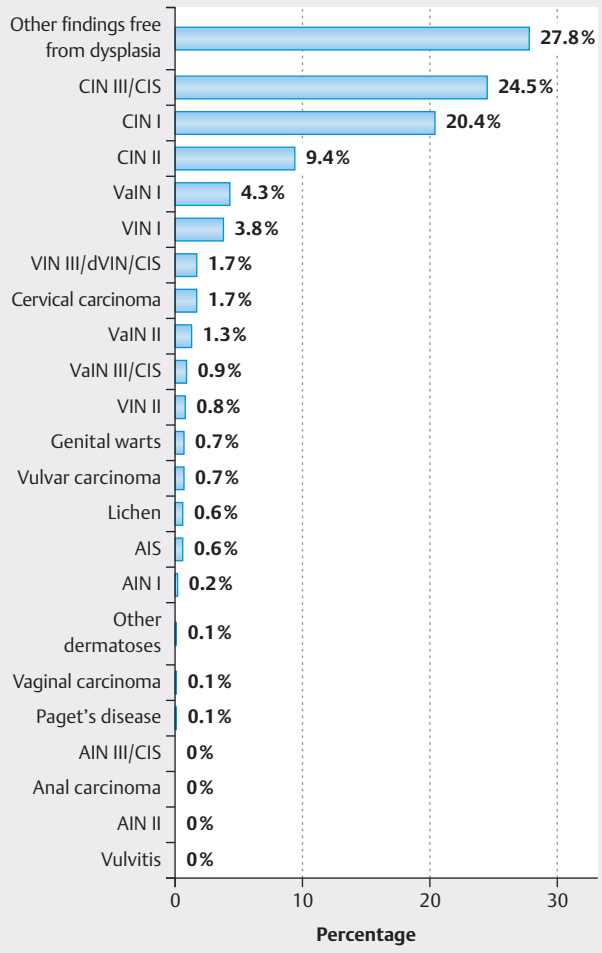
Dysplasia-free colposcopic findings were obtained in 57.7%. These included benign alterations with and without complaints such as treatment-resistant pruritus, recurring colpitides, postcoital bleeding, vulvodynia, chronic disease, congenital malformations, labial hypertrophy, or women with different forms of female genital mutation (FMG).

For the CIN2+ group (CIN II, CIN III, CIS: carcinoma in situ, AIS: adenocarcinoma in situ or cervical carcinoma), 2926 colposcopies showed a progression as a vulvar dysplasia, with VIN2+ observed in 72 and VaIN2+ observed in 81 colposcopies. In 23 colposcopies, synchronous or metachronous HSIL/carcinoma of the cervix, vagina, and vulva were observed in all three localizations.

The distributions of colposcopy results by localization showed that CIN III/HSIL was the second most frequent cervix biopsy observed. In other localizations of the vulva, vagina, and anus, HSIL was not always the most common observation following dysplasia-free findings (▶ **Fig. 5a–d**).

Histology

From a total of 4850 histologies, 27.8% did not involve dysplasia. Among mild, moderate, and severe dysplasia cases, cervical dysplasia was the most frequent at 54.9% (n = 2663 cases), followed by vaginal dysplasia at 6.5% (m = 316), just slightly ahead of vulvar dysplasia at 6.3% (n = 310). HSIL of the vulva (n = 124) was more frequent than HSIL of the vagina (n = 108); LSIL of the vulva was biopsied less frequently because it is more easy to assess. CIN I (LSIL) of the cervix was observed in 20.4% of cases (n = 989), and CIN II/CIN III/CIS/AIS (HSIL) of the cervix was observed in 34.5% of cases (n = 1674) (▶ **Fig. 6**). The distribution of histology results showed that in cervical biopsies in particular, CIN III/HSIL was observed more frequently than dysplasia-free findings. In the other localizations of the vulva, vagina, and anus, dysplasia-free findings or LSIL where the most frequent histological diagnoses (▶ **Fig. 7a–d**). These dysplasia-free findings included inflammatory changes/hyperkeratosis without other pathologies, scars, polyps, cysts or metaplasia.



▶ **Fig. 6** Histology results from the samples taken.

The most frequent histological diagnoses of benign conditions requiring treatment were lichen sclerosus/lichen ruber planus/simplex, and genital warts.

Therapeutic procedures

A total of 2009 patients underwent surgical procedures; these comprised 1641 surgeries on the cervix, 239 operations on the vulva, and 129 operations on the vagina. These are listed in ▶ **Fig. 8**, ▶ **Fig. 9**, and ▶ **Fig. 10**. Operations on the cervix, vulva, and vagina were divided into solely destructive laser evaporization procedures, and excision procedures. The indication for laser evaporization was determined based on histology, having previously excluded the possibility of (micro)invasion through colposcopy or vulvoscopy.

Contraindications for laser evaporization are confirmed AIS, TZ3 (transformation zone 3), age > 50, or a discrepancy between the colposcopy, cytology, and histology findings. Laser therapy is performed on areas showing abnormalities and on the cervical transformation zone. LOOP excision with laser evaporization and cervical curettage is a hybrid procedure involving both destructive techniques and excision techniques. In this procedure, a representative biopsy is taken from the punctum maximum of the HSIL using a small wire loop to remove surface material for additional histological confirmation of the lesion diagnosis. This is followed by cone-shaped laser evaporation of the wound bed and transformation zone in order to ensure a clinical Ris0 situation, as well as maximum destruction of HPV-infected cells. After every laser evaporization or conization procedure, cervical curettage is performed in order to further exclude the risk of endocervical dysplasia.

Key performance indicators

Within the scope of certification of a dysplasia unit, key performance indicators must be fulfilled [3].

KPI 4 covers the preoperative performance of a colposcopy for diagnostic clarification in the dysplasia unit following abnormal cytology results. The target is ≥ 95 % (▶ **Table 2**).

KPI 5 relates to the resection rate of ≥ CIN2 lesions, which should be as high as possible. The target is ≥ 85 % (▶ **Table 3**).

KPI 7 captures the proportion of R0 resections in surgeries performed on the cervix due to CIN III/ HSIL, and the target value is ≥ 80 % (▶ **Table 4**).

▶ **Table 2** Results for KPI 4 (Performance of a clarification colposcopy) for the period from 2015 to 2019 [20].

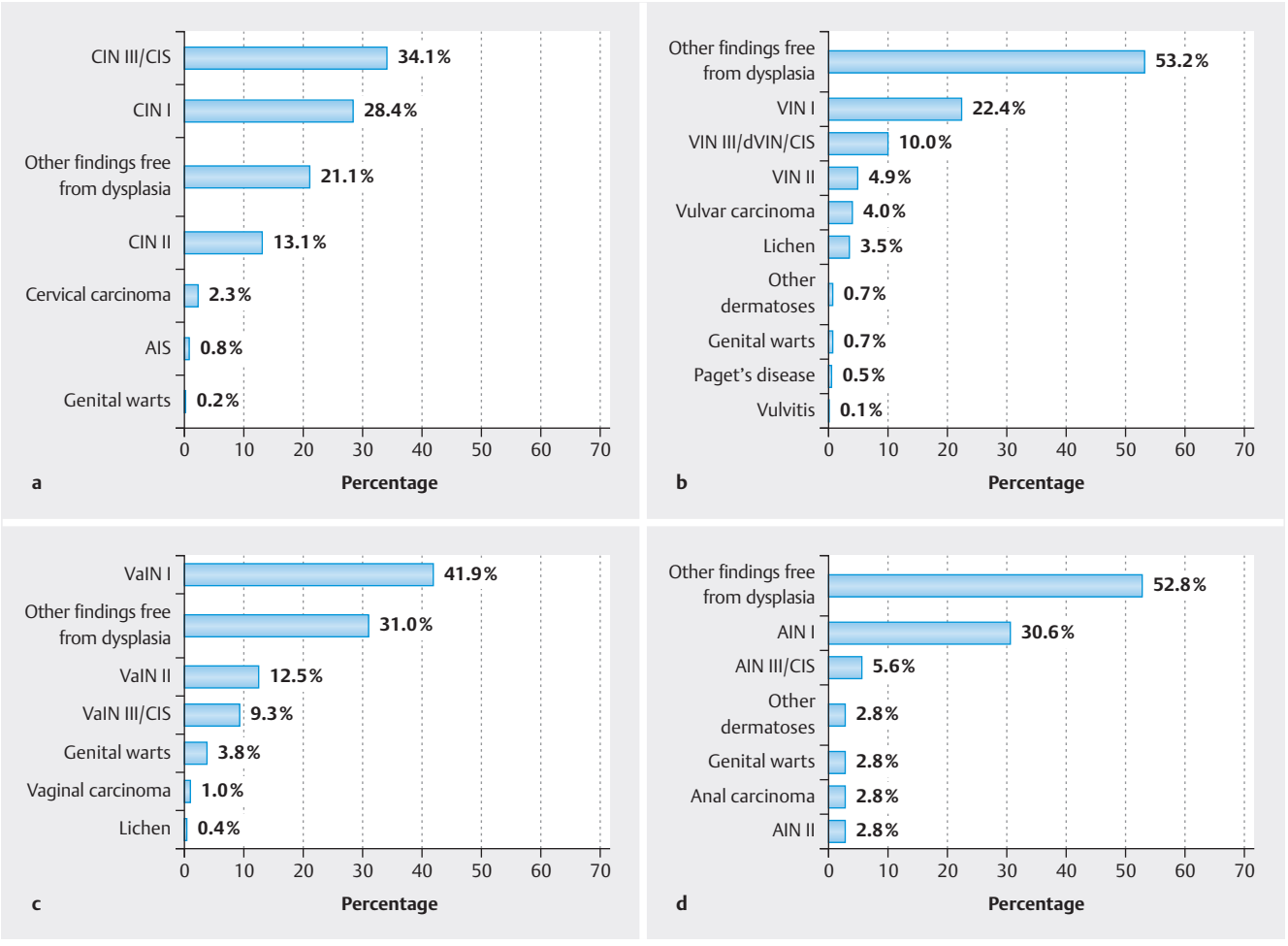
Year	2015	2016	2017	2018	2019
Rate	100 %	98.80 %	98.83 %	99.57 %	96.40 %

▶ **Table 3** Results for KPI 5 (excision with histology ≥ CIN II/HSIL) for the period from 2015 to 2019 [20].

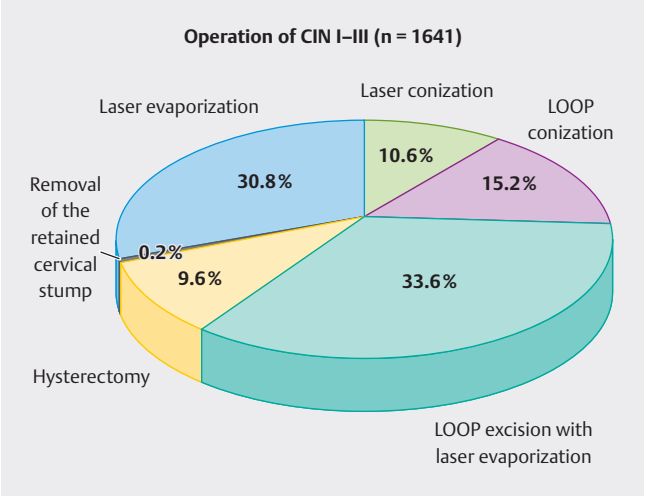
Year	2015	2016	2017	2018	2019
Rate	90.94 %	90.42 %	92.13 %	91.74 %	88.74 %

▶ **Table 4** Results for KPI 7 (proportion of R0 resections in CIN III/HSIL) for the period from 2015 to 2019 [20].

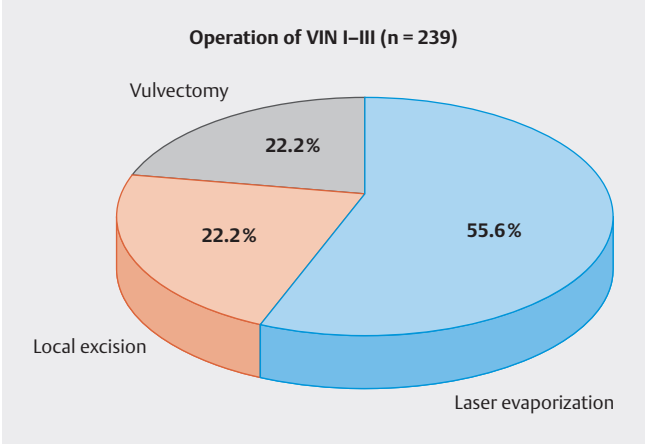
Year	2015	2016	2017	2018	2019
Rate	91.76 %	85.71 %	88.48 %	98.70 %	96.61 %



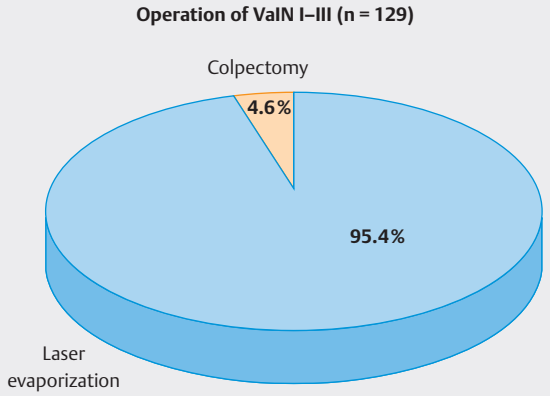
▶ **Fig. 7** Histology results from the samples taken according to localization. Cervix (**a**), vulva (**b**), vagina (**c**) or anus (**d**).



▶ **Fig. 8** Types of surgeries for CIN I–III.



▶ **Fig. 9** Types of operation on the vulva.



▶ **Fig. 10** Types of operation on the vagina.

Discussion

In our certified dysplasia unit, a standardized process for special outpatient care of genital dysplasia and diseases of the vulva and vagina has been established. This is based on the S3 guideline on prevention of cervical cancer (Working Group for Scientific Medical Societies (AWMF) registry number 015/027OL), the S3 guideline on diagnosis, therapy, and follow-up of cervical cancer (AWMF-Registernummer 032/033OL), the S2 k guideline on diagnosis, therapy, and follow-up care of vulvar cancer and its precursors (AWMF registry number 015/059, and the S2 k guideline on diagnosis, therapy and follow-up of vaginal cancer and its precursors (AWMF registry number 032/042) [21, 22, 23, 24].

The established concept of the dysplasia unit presented in this study was analyzed retrospectively. It provides a framework for the deployment of new screening strategies. Due to the fact that since 1 January 2020 low-risk groups (HPV high-risk positivity, group II-p, II-g, IIID1) should undergo colposcopy, the amount of referred patients has increased. To mitigate this, according to a statement by the AG-CPC, this patient cohort should only receive an early colposcopy if there is evidence of HPV type 16 or 18 [25]. Only time will tell the further development of screening algorithms for the prevention of cervical carcinoma after the initial evaluation of the screening program.

The certification process outlined is increasingly being considered by patients. In a multicenter study, 2500 patients were surveyed about their knowledge of certified centers during a 13-month period. In total, 53.4 percent of all surveyed patients understood the concept of a certified center, and 43.8 % reported that this was their (main) motivation for presenting to a certified center [26].

Quality criteria

The quality criteria for certification of a dysplasia unit include specific KPIs, with several of these exclusively applying to dysplasia units. These KPIs include a target rate of ≥ 95 % for performing preoperative colposcopies in all patients with abnormal cytology findings (KPI 4). The aim of a targeted colposcopy examination is to assess the maximum extent of the lesion, and thus to determine how it should be treated. This is consistent with results from the TOMBOLA studies, which also showed that performing colposcopies for diagnostic clarification can avoid overtreatment and associated unnecessary costs, as well as physical and psychological stress for patients [27, 28, 29]. Abnormal cytologic findings must be investigated preoperatively by colposcopy in accordance to guidelines in order to locate the dysplasia. A solely abnormal Pap smear without colposcopic examination is not an indication for surgery. Otherwise, if surgery is performed directly without colposcopy, dysplasias in unsuspected locations (e.g., ectocervical, vaginal, or vulvar dysplasia) may be missed, or unnecessary surgery may be performed on a regressive lesion [14].

KPI 5 for dysplasia units comprises maintaining a high resection rate for ≥ CIN2 lesions. Because of the possibility of spontaneous remission, CIN II/HSIL lesions should be examined at least every 24 months, depending on the age of the patient. In patients under 25 of age, CIN II/HSIL lesions must be examined at least every 24 months, and CIN III/HSIL lesions should be examined at least every 12 months [21, 22]. Due to their high regression rate of > 80%, surgery for CIN I/LSIL lesions should not be indicated directly [21, 22, 30]. If persisting, an ablation procedure should be favored instead of excision, depending on the transformation zone.

KPI 7 includes for the proportion of R0 resections in CIN III/HSIL lesions with a target of ≥ 80 %. Surgeries are performed with colposcopic monitoring in order to reduce the volume of resection, and at the same to time to increase the rate of Ris0 situations through targeted excision. In the case of laser evaporizations and LOOP excisions with laser evaporization, the extent of the in-sano region that needs to be removed with pathological CIN2+ lesions should be discussed, as laser evaporation of the transformation zone after excision should ensure a clinical Ris0 situation or allow any potential residual HSIL to resolve through immunological processes. In Ris1 situations without suspicion of invasive carcinoma, no immediate reoperation should be performed in accordance with the guidelines [21, 22]. Moreover, if the dysplasia expands to the ectocervical region, a significant tissue preservation can be achieved for the patient. Cervical curettage provides insight into the endocervical safety margin, while in the ectocervical region, colposcopy follow-up provides adequate certainty. In addition, the standardized co-testing follow-up at 6, 12, and 24 months, as specified in the guidelines, is highly sensitive for detecting either persistence or healing [21, 22].

Often, a cytology smear is not repeated in dysplasia units or consultations. However, it has been shown that only 47.65 % of smears taken in the context of routine monitoring correlate with colposcopy-guided Pap smears performed in a dysplasia unit as part of the diagnostic algorithm [8]. Therefore, a cytological smear and also an HPV-HR test in group I are taken again at first presentation at the Dysplasia Unit of the Erlangen University Hospital. The results in relation to colposcopy, cytological and histological results showed in own published evaluations that the detection rate of dysplasia of the cervix differs depending on the setting (routine versus further clarification). Colposcopy-guided Pap smears correlate significantly better to histology results than cytology smears taken in the context of routine screening without

colposcopy guidance [8]. Colposcopy-guided biopsies also play an important role in the detection of vaginal HSIL [10]. A combination of colposcopy findings, cytology, HPV PCR, and colposcopy-guided biopsy is required in order to correctly diagnose HSIL [12]. For this reason these results, which have already been published, are not discussed further in this article.

In general, type 1–3 excision is considered the gold standard [31]; however, the surgical procedure can be modified if the lesion is in an ectocervical location and/or in younger patients who plan to have children. For example, in younger patients planning to have children, laser evaporization with cervical curettage or a LOOP excision with peripheral laser evaporization and cervical curettage may be performed as the sole treatment, even in the presence of severe cervical dysplasia (CIN III/HSIL). However, this requires preoperative colposcopy to examine the transformation zone (TZ 1/2) and smear tests (Pap and HPV) in group ≤ IVa-p patients, as well as biopsy of the most conspicuous lesion to rule out (micro)invasion.

Colposcopic assessment itself is subjective and depends on the expertise of the physician performing the examination; for this reason, biopsies are indicated for diagnostic clarification of abnormal findings [12], and are consistent with the histology results from the operation in 71.9% of cases [10]. In any case, colposcopy and colposcopy-guided biopsies are low-risk forms of examinations whose rare side effects of pain, bleeding, anxiety or inflammation have been published [32]. In the authors' opinion, it is acceptable (including from a legal point of view) to perform this procedure with verbal consent from the patient without obtaining written consent, as it guarantees optimal diagnosis, thus enabling individualized therapy in accordance with the guidelines.

In our dysplasia unit, surgeries are performed under colposcopic guidance. After intraoperative application of Lugol's iodine, the majority of dysplasias can be demarcated, with the aid of preoperative marking, in order to work on the entire transformation zone with HPV-infected epithelial cells, reducing the volume of resected material, and defining the resection margins more precisely under colposcopic guidance.

In addition to solely dysplasia diagnostics, a special outpatient clinic is essential for patients with chronic complaints. Especially for patients with lichen sclerosus, lichen ruber planus, or chronic vulvitis, the initial diagnosis is often preceded by a long period of suffering. In patients with lichen sclerosus, it takes an average of five years to obtain an initial diagnosis. In these cases, interdisciplinary cooperation between the various specialties involved can often lead to a faster diagnosis and better treatment for the patient. In cases of chronic vulvitis, severe forms of lichen sclerosus, or genital atrophy, fractional CO_2 laser therapy of the vulva and/or vagina can be offered as a treatment option. This procedure creates needle-prick-like microwounds in the epidermis which lead to contraction and regeneration of collagen fibers, angiogenesis, increased blood circulation, and stimulation of growth factors. These increase the elasticity of the skin [33, 34, 35]. However, there is currently no long-term follow-up data.

Conclusion

This retrospective analysis of our dysplasia unit provides a framework for the deployment of new screening strategies. However, improvements to the existing structures are essential, particularly since patient numbers are expected to significantly increase following the new decision of the Federal Joint Committee. There is also a need for discussing the further procedure after clarification colposcopy; this issue is not yet addressed in the current G-BA algorithm for diagnostic clarification. The recommendation for (persistent) cytological abnormalities or persistent HPV positivity remains unclear and needs to be discussed.

Conflict of Interest

The authors declare that they have no conflict of interest.

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