The Highly Protective Effect of Newborn Circumcision Against Invasive Penile Cancer

Edgar J. Schoen, MD; Michael Oehrli, MPA, CTR; Christopher J. Colby, PhD; and Geoffrey Machin, MD

ABSTRACT. Objective. We determined the relation between newborn circumcision and both invasive penile cancer (IPC) and carcinoma in situ (CIS) among adult male members of a large health maintenance organization.

Subjects and Methods. Circumcision status was ascertained by a combination of pathology reports, medical record review, and questionnaires for 213 adult male members of a large prepaid health plan who were diagnosed with IPC or CIS.

Results. Of 89 men with IPC whose circumcision status was known, 2 (2.3%) had been circumcised as newborns, and 87 were not circumcised. Of 118 men with CIS whose circumcision status was known, 16 (15.7%) had been circumcised as newborns.

Conclusions. Our results confirm the highly protective effect of newborn circumcision against IPC and the less protective effect against CIS. Pediatrics 2000;105(3).

ABBREVIATIONS. UTI, urinary tract infection; HIV, human immunodeficiency virus; STD, sexually transmitted disease; IPC, invasive penile cancer; CIS, carcinoma in situ; KP, Kaiser Permanente Medical Care Program of Northern California; SEER, Surveillance, Epidemiology, and End Results.

METHODS

This retrospective case ascertainment study reviewed clinical information for patients diagnosed with IPC or CIS from 1954 through 1997 while these patients were members of the Kaiser Permanente Medical Care Program of Northern California (KP), a large health maintenance organization that serves 2.8 million members.

The State of California mandated cancer reporting in 1988. Because not all KP facilities reported their cancer cases from 1954 through 1987, cases from that period could not be used to determine incidence of IPC. Ascertainment of cases from the KP Northern California Region was complete for the 10-year period from 1988 through 1997. Diagnosis of IPC versus CIS was based on the original pathology reports. In questionable cases, the microscopic sections were reviewed by 1 of the authors (G.M.).

Clinical information was determined from pathology reports, review of individual medical charts, as well as from the KP computerized database, which uses International Classification of Diseases, Ninth Revision codes for hospitalizations and KP Outpatient Summary Clinic Record codes for outpatient visits.

All cases were identified through the population-based KP Cancer Registry, which receives data from 18 KP medical centers and 15 KP outpatient clinics in Northern California and is part of the California State Cancer Reporting System. The KP Registry receives >14 000 new cases annually—approximately 30% of all cancer cases reported in the San Francisco Bay Area—and is part of the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. Coupled with internal KP quality control mechanisms, periodic retrospective audits by both the SEER program, and the California Cancer Registry ensure that completeness of case reporting exceeds 97%. Moreover, the KP member population closely reflects the racial and ethnic diversity of the general California population and contains sufficient numbers of rarer cancers, such as penile cancer, for study.

Circumcision status was initially determined through review of individual medical charts and pathology reports. A patient questionnaire was sent in 3 mailings at 2-week intervals to further confirm circumcision status in these patients.

RESULTS

The 213 cases included 122 CIS and 91 IPC cases, a ratio of 1.3:1 for the period from 1954 through 1997.
TABLE 1. Frequency and Anatomic Site of IPC and CIS Among 213 Adult Male Members of KP Health Plan as Reported From 1954 Through 1997

<table>
<thead>
<tr>
<th>Time span</th>
<th>No. (%) of Patients With IPC</th>
<th>No. (%) of Patients With CIS</th>
<th>Total No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1954–1987</td>
<td>32 (42)</td>
<td>45 (58)</td>
<td>77 (100)</td>
</tr>
<tr>
<td>1988–1997</td>
<td>59 (43)</td>
<td>77 (57)</td>
<td>136 (100)</td>
</tr>
<tr>
<td>Total cases</td>
<td>91 (43)</td>
<td>122 (57)</td>
<td>213 (100)</td>
</tr>
<tr>
<td>Anatomic site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glans</td>
<td>41 (45)</td>
<td>16 (13)</td>
<td></td>
</tr>
<tr>
<td>Prepuce</td>
<td>13 (14)</td>
<td>12 (10)</td>
<td></td>
</tr>
<tr>
<td>Overlapping</td>
<td>2 (2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Body</td>
<td>4 (5)</td>
<td>6 (5)</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>31 (34)</td>
<td>88 (72)</td>
<td></td>
</tr>
</tbody>
</table>

*Median age at diagnosis: 65 years.
†Median age at diagnosis: 58 years.

The rarity of newborn circumcision among patients with IPC in our study (2 in 89 invasive cancer cases) warrants specific description of advanced age of onset and mild manifestations. In 1 patient, a large lesion (1.8 cm × 1.8 cm × 0.6 cm) located on the shaft of the penis was diagnosed in 1991, when the patient was 79 years old. The histologic report showed combined Bowen’s disease and moderately differentiated, superficially infiltrating squamous cell carcinoma.

Median age at diagnosis, 5-year relative survival rates, and incidence of IPC in our KP series were consistent with data reported by the State of California and SEER (Table 4).

The overwhelming evidence of the role of the foreskin in the pathogenesis of the invasive forms of penile cancer, and the protective effect of early circumcision against penile cancer has long been recognized and has been cited as a major medical rationale for recommending universal newborn circumcision. A 1991 review noted that 592 IPC cases reported from 5 major cancer centers in the United States included no men circumcised in infancy despite the >50% prevalence of newborn circumcision among US men by the mid-1950s and peak prevalence of >80% by the 1960s. Although >50,000 US men are estimated to have been diagnosed with IPC during a 55-year period, only 10 case reports have noted that affected men were circumcised as infants. However, no population-based studies associating circumcision and penile cancer have appeared, and IPC in circumcised men is probably underreported.

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skin in penile cancer was questioned by a 1993 case-control report that found that although absence of neonatal circumcision was associated with increased risk of penile cancer, the association was much weaker than previously thought: the odds ratio reflected a 3.2-fold increased risk in uncircumcised men. However, an accompanying editorial critiqued a study for combining IPC and CIS under the term penile cancer unlike the previous series which included only IPC.

Our results confirm the highly protective effect of newborn circumcision against IPC. Considering the reported US circumcision rate of 50% in the 1930s (the median birth date of our IPC patients), relative risk of IPC for uncircumcised to circumcised men is 22:1. Reports of ~1400 cases of IPC annually in the United States suggest the potential to reduce this number to <70 cases annually if all men were circumcised. In contrast, if all US men were uncircumcised, this number could increase to >2800 cases annually.

Combining CIS with IPC for analysis is not justifiable. IPC is a potentially lethal disease whose relative 5-year survival rate is 65% nationally and 72% in our patients; CIS is an easily treatable, nonlethal disease. Penile CIS is not included when calculating penile cancer incidence rates. In contrast to the rarity of IPC in uncircumcised men, CIS is not uncommon in uncircumcised men as was true in our series. Further, CIS is a heterogeneous disorder whose most benign form is bowenoid papulosis (penile intraepithelial neoplasia); this classification represents less aggressive disease than Bowen’s disease or Queyrat’s erythroplasia.

In a review of bowenoid papulosis, Patterson et al noted that CIS has never been found to progress to IPC and occurs in circumcised as well as uncircumcised men. Malek et al found that newborn circumcision was associated with minor-grade CIS lesions but not with major-grade CIS or IPC. These authors found that circumcision performed during the neonatal period (but not later in life) gave almost total protection against invasive squamous cell penile carcinoma. The authors concluded that presence of the foreskin, particularly when phimotic, exposes the preputial cavity to many carcinogenic factors and that even high standards of hygiene do not fully protect uncircumcised men.

Our findings confirm the results of earlier studies that indicate the overwhelming predominance of IPC in uncircumcised men. Our study also calls into question the more recent claim of less protection afforded by circumcision against penile cancer; that claim was made based on combining IPC and CIS and we believe that this combination is not valid.

The initial decision to perform newborn circumcision as a preventive health measure in US newborn boys began around the turn of the century. By the 1930s, the newborn circumcision rate exceeded 50% and increased evidence was developing of protection against penile cancer and promotion of improved genital cleanliness, ease of hygiene, prevention of foreskin infection (balanoposthitis), and phimosis. More recently, compelling evidence has shown that newborn circumcision prevents UTI, primarily in the first year of life, and also prevents certain STDs in men, particularly HIV and genital ulcer disease.

The incidence of penile cancer around the world is related to a combination of circumcision status and proper hygiene and varies from .1 case per 100 000 in Israel (where circumcision is almost universal) to 1 case per 100 000 in Denmark (where circumcision is not usually performed but hygiene is good) to 4.2 cases per 100 000 in countries such as Paraguay, where neither newborn circumcision nor adequate hygiene is common. Thus, incidence can differ more than 40-fold between countries. Penile carcinoma is the most common cancer among Ugandan men and constitutes 17% of all malignancies in some areas of Brazil. Kochen and McCurdy stated that the similar incidence of penile cancer in the United States and Denmark is misleading because in the United States, the rate of circumcision is high and penile cancer is essentially limited to uncircumcised US men, whose hygiene is apparently worse than in Danish men. Further, the authors pointed out that annual incidence rates do not address the lifetime risk of penile cancer. Based on life–table analysis, the authors estimated that risk to be 1 in 600 for uncircumcised men in the United States. International cancer

<table>
<thead>
<tr>
<th>Type of IPC (n = 91)</th>
<th>No. (%) of Patients Affected</th>
<th>Type of CIS (n = 122)</th>
<th>No. (%) of Patients Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell cancer</td>
<td>77 (85)</td>
<td>Bowen’s disease</td>
<td>54 (44)</td>
</tr>
<tr>
<td>Verrucous cancer</td>
<td>7 (8)</td>
<td>Squamous cell CIS</td>
<td>44 (36)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>3 (3)</td>
<td>CIS, not specified</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Fibroblastic osteosarcoma</td>
<td>1 (1)</td>
<td>Queyrat’s erythroplasia</td>
<td>9 (7)</td>
</tr>
<tr>
<td>Infiltrating duct cancer</td>
<td>1 (1)</td>
<td>Transitional cell CIS</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Malignant fibrous histiocytoma</td>
<td>1 (1)</td>
<td>Papillary CIS</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Carcinoma, not specified</td>
<td>1 (1)</td>
<td>Melanoma CIS</td>
<td>1 (&lt;1)</td>
</tr>
</tbody>
</table>

TABLE 4. Comparative Data Reported by State of California, National Cancer Institute SEER and KP for IPC

<table>
<thead>
<tr>
<th>KP</th>
<th>SEER12</th>
<th>State of California11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at diagnosis (y), 1991–1995</td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>5-y relative survival rates (%), 1989–1994</td>
<td>72</td>
<td>65</td>
</tr>
<tr>
<td>Incidence (no. of cases per 100 000 men), 1991–1995</td>
<td>.7</td>
<td>.7</td>
</tr>
</tbody>
</table>
TABLE 5. Comparison of Invasive Penile Cancer Incidence in Five Countries*

<table>
<thead>
<tr>
<th>Country</th>
<th>No. Cases per 100,000 Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>.1</td>
</tr>
<tr>
<td>Denmark</td>
<td>.6</td>
</tr>
<tr>
<td>Germany (GDR)</td>
<td>.9</td>
</tr>
<tr>
<td>Paraguay</td>
<td>.2</td>
</tr>
<tr>
<td>United States (total)</td>
<td>.6</td>
</tr>
<tr>
<td>United States (Puerto Rican)</td>
<td>3.0</td>
</tr>
<tr>
<td>United States (Filipino)</td>
<td>.1</td>
</tr>
</tbody>
</table>

* Adapted and reproduced by permission of the publisher from Cancer incidence in 5 continents. Age-standardized incidence rates, 4-digit rubrics, and age-standardized and cumulative incidence rates, 3-digit rubrics.35

incidence data for 199235 (Table 5) showed that in the Western European countries of Denmark and Germany, where newborn circumcision is rarely performed, penile cancer rates were 10-fold higher than in Israel, where virtually all newborn boys are circumcised. The overall penile cancer incidence in the United States (0.6) represents a combination of uncircumcised and circumcised men and thus is between the incidence in Israel (0.1) and the incidence in Denmark (1.0). Incidence in the United States varies 30-fold among ethnic groups and ranges from 0.1 in Filipino men, whose culture includes circumcision, to 3.0 in Puerto Rico, where men are not circumcised.35

In counseling new parents who are contemplating circumcision for their newborn boys, physicians and other health care providers should be aware of the preventive health benefits occurring over a boy’s lifetime: protection against UTI in the first year of life, decreased risk of phimosis and balanoposthitis in early childhood, and prevention of HIV and other STDs in early adulthood. Our study shows that the highly protective effect against IPC in middle and old age should also be part of this lifetime decision and should be pointed out during counseling.

ACKNOWLEDGMENTS

The research was supported by an innovation grant from The Permanente Medical Group.

The Medical Editing Department of Kaiser Foundation Research Institute provided editorial assistance.

REFERENCES

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