Correlation between treatment modality and response to therapy in two histopathological types of cervical cancer

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Abstract. Cervical cancer is the second commonest cancer in Indonesia, with 2,638 cases reported in 2008. Most therapeutic recommendations currently address squamous cell carcinomas, and some studies suggest that adenocarcinomas exhibit poor response to treatment. This study aimed to examine the correlation between the histopathological types of cervical cancer and response to therapy and to compare the responses to different treatment modalities. This cross-sectional study included secondary data of patients diagnosed with stage IIB-IIIB cervical cancer between 2011–2013 at Cipto Mangunkusumo Hospital who underwent radiation and chemoradiation. Of the 163 patients included in this study, 107 presented with squamous cell carcinoma and 56 with adenocarcinoma. No significant differences in response to therapy were observed between the two histopathological types. Moreover, 67.5% patients received radiation only, whereas 32.5% received concurrent chemoradiation therapy using a platinum-based agent. Among those treated with chemoradiation, 98.1% exhibited complete response, whereas only 72.7% of those receiving radiation exhibited complete response. Irrespective of the treatment type, no differences in the response to therapy were observed between patients with squamous cell carcinoma and adenocarcinoma. Moreover, chemoradiation appeared to induce a better response compared with only radiation in all patients.

1. Introduction
Cervical cancer is the third commonest cancer in women, with approximately 5,30,000 cases and 2,75,000 (52%) deaths being reported in a year [1]. In Indonesia, data from thirteen pathological anatomy examination centers suggested that cervical cancer is the second commonest cancer overall, with approximately 2,638 cases reported in 2008 [2]. Moreover, approximately 76% of these patients presented at an advanced stage [3], which complicated treatment options and decreased survival rates [4].

Most therapeutic recommendations currently address squamous cell carcinomas because the natural history of adenocarcinomas is still not completely understood [5]. However, the need to differentiate treatment strategies by histopathological type is still debatable, with some studies reporting that adenocarcinomas exhibit a poorer response to therapy, worse prognosis, and lower survival rates than squamous cell carcinomas [5-8]. The present study aimed to examine the correlation between the histopathological type of cervical cancer (squamous cell carcinoma or
adenocarcinoma) and the response to therapy and to also compare the responses to different treatment modalities (radiation only and chemoradiation).

2. Methods
This cross-sectional study included secondary data from medical records of patients who presented with stage IIB-IIIB cervical cancer between 2011 and 2013 at the Oncology and Gynecology Polyclinic, Cipto Mangunkusumo Hospital and underwent radiation and chemoradiation therapy. The inclusion criteria were as follows: diagnosis of stage IIB-IIIB cervical cancer, squamous cell carcinoma or adenocarcinoma, no involvement of para-aortic lymph nodes (as detected by ultrasonography), treatment including radiation only or chemoradiation concurrent with platinum chemotherapy regimen only or in combination, and patients who had completed the treatment regimen. The exclusion criteria were as follows: patients with progressive or recurrent cervical cancer, patients that had not completed the radiation therapy or chemoradiation protocol, and patients who had previously undergone surgical treatment.

3. Results
This study included 163 patients, 107 of whom presented with squamous cell carcinoma (SCC) and 56 presented with adenocarcinoma (AC) (Table 1).

Table 1. Patient demographics

| Category                              | SCC (n = 107) | AC (n = 56) | n  | p   |
|---------------------------------------|---------------|-------------|----|-----|
| Age (Mean ± SD)                       | 52.56 ± 7.807 | 50.46 ± 7.701 | 0.104 |     |
| Stage                                 |               |             |    |     |
| IIB                                   | 28 (26.2%)    | 25 (44.6%)  | 53 (32.5%) | 0.027 |
| IIIB                                  | 79 (73.8%)    | 31 (55.4%)  | 110 (67.5%) |     |
| Differentiation Grade                 |               |             |    |     |
| Good                                  | 26 (24.3%)    | 29 (51.8%)  | 55 (33.7%) | 0.000 |
| Average                               | 68 (63.5%)    | 16 (28.6%)  | 84 (51.5%) |     |
| Bad                                   | 13 (12.2%)    | 11 (19.6%)  | 24 (14.7%) |     |
| Tumor Size                            |               |             |    |     |
| >4.0                                  | 61 (57.0%)    | 35 (62.5%)  | 96 (58.9%) | 0.611 |
| ≤4.0                                  | 46 (43.0%)    | 21 (37.5%)  | 67 (41.1%) |     |
| Lymphovascular Space Invasion         |               |             |    |     |
| Positive                              | 11 (10.3%)    | 4 (7.1%)    | 15 (9.2%) | 0.709 |
| Negative                              | 96 (89.7%)    | 52 (92.9%)  | 148 (90.8%) |     |
| Pelvic Lymph Node Enlargement         |               |             |    |     |
| Positive                              | 13 (12.1%)    | 4 (7.1%)    | 17 (10.4%) | 0.469 |
| Negative                              | 94 (87.9%)    | 52 (92.9%)  | 146 (89.6%) |     |
| Therapy Modality                      |               |             |    |     |
| Radiation                             | 78 (72.9%)    | 32 (57.1%)  | 110 (67.5%) | 0.602 |
| Chemoradiation                        | 29 (27.1%)    | 24 (42.9%)  | 53 (32.5%) |     |
The association between histopathological type and response to therapy is shown in Table 2. Among patients treated with chemoradiation, 98.1% exhibited complete response, whereas only 72.7% receiving radiation only exhibited complete response (p < 0.001) (Table 3).

### Table 2. Association between histopathological type and response to therapy

| Histopathology | Response to Therapy | Total | p value | OR (95% CI) |
|----------------|---------------------|-------|---------|-------------|
|                | Partial | Complete | n | % | n | % | n | % |    |
| SCC            | 19  | 17.8 | 88 | 82.2 | 107 | 100 | 0.721 | 0.792 | (0.353–1.776) |
| AC             | 12  | 21.4 | 44 | 78.6 | 56 | 100 |      |      |      |
| Total          | 31   | 19.0 | 132 | 81.0 | 163 | 100 |      |      |      |

SCC: Squamous Cell Carcinoma  
AC: Adenocarcinoma

### Table 3. Association between treatment modality and response to therapy

| Treatment Modality | Response to Therapy | Total | p value | OR (95% CI) |
|--------------------|---------------------|-------|---------|-------------|
|                    | Partial | Complete | n | % | n | % | n | % |    |
| Radiation          | 30  | 27.3 | 80 | 72.7 | 110 | 100 | 0.001 | 19.500 | (2.580–147.398) |
| Chemoradiation     | 1   | 1.9 | 52 | 98.1 | 53 | 100 |      |      |      |
| Total              | 31   | 19.0 | 132 | 81.0 | 163 | 100 |      |      |      |

No significant differences in response to radiation and chemoradiation were observed between the two histopathological types (Table 4 and 5). Meanwhile, in patients with chemoradiation type, the histopathological type did not show therapy response.

### Table 4. Association between histopathological type and response to therapy in the radiation only group

| Histopathology | Response to Therapy | Total | p value | OR (95% CI) |
|----------------|---------------------|-------|---------|-------------|
|                | PR | CR | n | % | n | % | n | % |    |
| SCC            | 18 | 23.1 | 60 | 76.9 | 78 | 100 | 0.191 | 2.000 | (0.822–4.864) |
| AC             | 12 | 37.5 | 20 | 62.5 | 32 | 100 |      |      |      |
| Total          | 30 | 27.3 | 80 | 72.7 | 110 | 100 |      |      |      |

SCC: Squamous Cell Carcinoma  
AC: Adenocarcinoma

### Table 5. Association between histopathological type and response to therapy in the chemoradiation group

| Histopathology | Response to Therapy | Total | p value | OR (95% CI) |
|----------------|---------------------|-------|---------|-------------|
|                | Partial | Complete | n | % | n | % | n | % |    |
| SCC            | 1   | 3.4 | 28 | 96.6% | 29 | 100 | 1.000 | 1.036 | (0.967–1.109) |
| AC             | 0   | 0 | 24 | 100% | 24 | 100 |      |      |      |
| Total          | 1   | 1.9 | 52 | 98.1 | 53 | 100 |      |      |      |

SCC: Squamous Cell Carcinoma  
AC: Adenocarcinoma
4. Discussion
This study found no significant differences in age were observed between the two histopathological types. Moreover, an insignificant difference in response to therapy was observed between the squamous cell carcinomas and adenocarcinomas (82.2% and 78.6%, respectively; p = 0.721). This result contradicted the results of a previous study conducted by Katanyoo et al. who reported that squamous cell carcinoma patients exhibited a better response (94.7%) to radiotherapy and chemoradiation than adenocarcinoma patients (86.5%) [5].

On comparing the response to different treatment modalities between patients with squamous cell carcinomas and those with adenocarcinomas, no significant differences were observed. This finding could be explained by the greater grade of differentiation exhibited by adenocarcinomas than by squamous cell carcinomas.

5. Conclusion
In conclusion, the findings of this study showed no differences in the response to therapy between patients with squamous cell carcinoma and those with adenocarcinoma, irrespective of the treatment type (radiation only or chemoradiation). Moreover, chemoradiation appeared to induce a better response compared with radiation only in all patients.

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