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JAPAN EXPERIENCE WITH THE FIGO 2000 SCORING SYSTEM AND THE CHORIOCARCINOMA RISK SCORE TABLE

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8.1 INTRODUCTION

Gestational trophoblastic neoplasia (GTN) includes invasive moles, choriocarcinoma, and placental site trophoblastic tumors (PSTTs). With the introduction of effective chemotherapy regimens, highly sensitive human chorionic gonadotropin (hCG) measurement and adequate clinical classification of GTN, excluding PSTT, almost all patients with low-risk GTN and 80-90% of patients with high-risk GTN can now attain remission.

Several clinical classification systems for GTN have been reported and are now in use[1-4], but differences between these scoring systems regarding the definition of GTN make comparisons of data from different centers extremely difficult. In 2000, the new International Federation of Gynecology and Obstetrics (FIGO) anatomical staging and risk factor scoring system was adopted.[5] This system was expected to promote the uniform reporting of clinical data throughout the world and to help physicians decide upon optimal treatment regimens. However, McGrath et al.[6] recently reported that only 30% of patients with a FIGO score of 5-6 are cured with single-agent chemotherapy due to development of drug resistance.

The original classification system for GTN (the choriocarcinoma risk score table) is still being used in Japan (Table 1). We attempted to estimate the pathological diagnosis of GTN patients using features of this original system that are similar to those of the FIGO 2000 risk factor scoring system. For patients with a GTN score of 5 or higher, the sensitivity, specificity, and positive and negative predictive value for pathologically confirmed choriocarcinoma were reported to be 92.2%, 93.5%, 91.4% and 94.1%, respectively.[4]

In this chapter, the optimal treatment of patients with GTN classified according to both the FIGO 2000 scoring system and the choriocarcinoma risk score table is compared.

8.2 PATIENTS WITH GTN

Between 1974 and 2011, 457 women with GTN were treated at Chiba University and Tokyo Women's Medical University. Definite lesions could not be detected in 14 patients using several imaging modalities, and these patients were subsequently excluded from the analysis. The remaining 443 patients were diagnosed with clinical choriocarcinoma (n=105) or a clinical invasive mole (n=338) using the choriocarcinoma risk score table. One hundred and five patients with clinical choriocarcinoma (scored ≥5) were treated using a combination chemotherapy regimen, whereas the 338 patients with a clinical invasive mole (scored < 5) were initially started on a single-agent chemotherapy regimen. All these 443 GTN patients were retrospectively reassessed according to the FIGO 2000 risk factor scoring system, and FIGO scores for clinical invasive moles and clinical choriocarcinoma were ranged from 0 to 9 (mean±SD, 2.5±1.5), and from 2 to 17 (mean±SD, 8.3±2.9), respectively (Figure 1). Three patients (0.9%) with a clinical invasive mole had scores of ≥7 and 27 patients (25.7%) with clinical choriocarcinoma had scores of <7 scored, respectively. The most important differences between the choriocarcinoma risk score table and the FIGO risk factor scoring system were weighting applied to term pregnancy (5 points vs. 2 points) and the presence of regular menstrual cycles after the termination of the previous pregnancy (5 points vs. none).

Score	0	1	2	3	4	5
Antecedent pregnancy	Hydatidiform mole			Abortion		Term
Intervals months from index pregnancy	< 6				6 ～< 36	≧36
Pre-treatment hCG (mIU/ml)	$< 10^6$	10^6 ～ $<10^7$		$\geqq 10^7$		
Primary lesion	Uterine corpus Parametrium Vagina			Ovary Tube	Uterine cervix	Extra pelvic
Site of metastases	None, Lung Intrapelvic					Extra pelvic except lung
Pulmonary metastases						
Largest tumor size	< 20 mm			20 ～< 30 mm		≧30 mm
Uniformity	Uniform				Non-uniform	
Number	≦20					>21
Menstrual cycles	Irregular					Regular
Score	0	1	2	3	4	5

Table 8.1 Choriocarcinoma risk score table

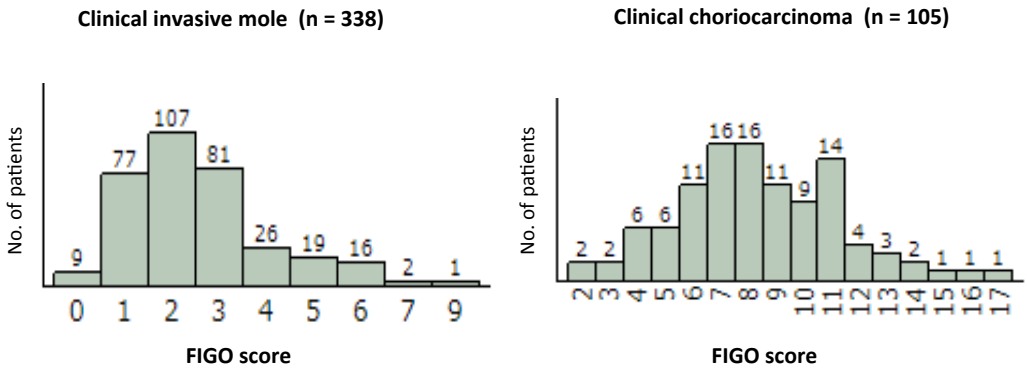

Figure 8.1

(A) International Federation of Gynecology and Obstetrics (FIGO) scores of clinical invasive moles ranged from 0 to 9 (mean±SD: 2.5±1.5). Three patients (0.9%) were classified as having high-risk GTN according to the FIGO system.

(B) FIGO scores of clinical choriocarcinoma ranged from 2 to 17 (mean±SD: 8.3±2.9). Ten patients (9.5%) and 17 patients (16.2%) were classified as low-risk GTN and high-risk GTN, respectively, according to the FIGO system.

8.2.1

DRUG RESISTANCE, PRIMARY REMISSION AND RELAPSE RATES

The drug resistance, primary remission and relapse rates of GTN patients according to the two scoring systems are summarized in Table 2. Drug resistance was defined as a leveling out of hCG titers (a less than 50% reduction) over at least 2 consecutive cycles of chemotherapy or an increase in hCG levels. Primary remission was defined as normal hCG levels for at least 3 consecutive weekly measurements.

There were no significant differences between the drug resistance (25.7% vs. 28.4%), primary remission (90.4% vs. 88.9%) and relapse rates (12.5% vs. 13.7%) of patients with clinical choriocarcinoma and FIGO high-risk, respectively. Moreover, there were also no significant differences between the drug resistance (12.4% vs. 12.7%), primary remission (100% vs. 99.7%) and relapse rates (2.4% vs. 3.3%) of patients with a clinical invasive mole and FIGO low-risk, respectively.

However, 27 patients classified as FIGO low-risk and 3 patients as high-risk were initially treated with combination chemotherapy and single-agent chemotherapy, respectively, based on our original classification

a) Classification based on the choriocarcinoma risk score table	**Cases N (%)**
Clinical choriocarcinoma	105
Developing drug resistance	27 (25.7)
Primary remission	95 (90.4)
Relapsed	13 (13.7)
Clinical invasive mole	338
Developing drug resistance	42(12.4)
Primary remission	338(100)
Relapsed	8 (2.4)

b) Classification based on the FIGO 2000 scoring system	Cases N (%)
FIGO high-risk	81
Developing drug resistance	23(28.4)
Primary remission	72(88.9)
Relapsed	9 (12.5)
FIGO low-risk	362
Developing drug resistance	46(12.7)
Primary remission	361(99.7)
Relapsed	12 (3.3)

Table 8.2 Drug resistance, primary remission and relapse rates of GTN classified by choriocarcinoma risk score table (a) and FIGO 2000 scoring system (b)

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8.2.3 TREATMENT OF PATIENTS WITH FIGO SCORES 5–6

Of these 362 patients with low-risk GTN, 52 patients (14.4%) had FIGO scores of 5–6 and 310 patients (85.6%) had scores of 0–4 (Table 3). Among these 52 patients with FIGO scores of 5–6, 17 patients were diagnosed as having clinical choriocarcinoma based on the choriocarcinoma risk score table and were initially treated with combination chemotherapies. Three patients (17.6%) developed drug resistance to the first line combination chemotherapy. Although 2 patients attained primary remission with second line combination chemotherapies, one patient developed multi-drug resistance and died. Moreover, despite the small patient numbers, the relapse rate for these 16 remitting patients with clinical choriocarcinoma was also high (4/16: 25.0%), despite their initial treatment with combination chemotherapy.

Conversely, the remaining 35 patients with FIGO scores of 5–6 were initially treated with single-agent chemotherapies based on the choriocarcinoma risk score table. All patients achieved eventual remission, though 5 patients (14.3%) required a change

in chemotherapy regimen because of drug resistance. The relapse rate was also low (5.7%) compared to that of patients with clinical choriocarcinoma (25.0%).

Furthermore, if this comparison was restricted to the 335 patients with a clinical invasive mole, the drug resistance rate of patients with FIGO scores of 5–6 and 0–4 were not significantly different (14.3% vs. 12.3% P=0.75), even amongst patients initially treated with single agent chemotherapy.

	FIGO 5-6 (n = 52)	FOGO 0-4 (n = 310)
Clinical choriocarcinoma	17	10
Drug resistance	3 (17.6)	1 (10.0)
Primary remission	16 (94.1)	10 (100)
Relapse	4 (25.0)	0
Clinical invasive mole	35	300
Drug resistance	5 (14.3)	37 (12.3)
Primary remission	35 (100)	300 (100)
Relapse	2 (5.7)	6 (2.0)

( ): %

Table 8.3 Drug resistance and relapse rates of FIGO low-risk patients classified by choriocarcinoma risk score table

8.3 DISCUSSION

GTN is highly sensitive to chemotherapy and the prognosis of low-risk patients is excellent when treated with single-agent chemotherapy (MTX, Act-D, or etoposide). However, the most appropriate chemotherapy regimen for low-risk patients continues to be debated, with MTX currently being the preferred regimen in terms of short- and long-term side effects. However, McGrath et al.[6] recently reported that only 30% of patients with a FIGO score of 5-6 could be cured with these single-agent chemotherapy regimens because of the development of drug resistance.

In Japan, GTN classification has been based on the choriocarcinoma risk score table combined with the FIGO 2000 risk factor scoring system[4]. The former is used to estimate the pathological diagnosis of GTN based on several clinical factors, including the type of antecedent pregnancy, the latent period from the antecedent pregnancy, the pretreatment hCG titers, the primary lesion, metastatic sites, the size, shape, and number of pulmonary metastases, and the regularity of menstrual cycles after the termination of the previous pregnancy - similar to the FIGO 2000 risk factor scoring system. For patients with a score of 5 or more based on the choriocarcinoma risk score table, initial combination chemotherapy is recommended.

In this study, 105 patients with a FIGO score between 2 and 17 (mean±SD: 8.3±2.9) and 338 patients with a FIGO score between 0 and 9 (mean±SD, 2.5±1.5) were classified as having a clinical choriocarcinoma or a clinical invasive mole, respectively, based on the choriocarcinoma risk score table. The former group was initially treated with combination chemotherapy and the latter group was initially treated with single-agent chemotherapy. Even when the combination chemotherapy was administered, the drug resistance and relapse rates of patients with clinical choriocarcinoma were significantly higher than those of patients with a clinical invasive mole (25.7% vs. 12.4%, p=0.01; and 13.7% vs. 2.4%, P=0.001, respectively). The drug resistance and relapse rates of patients with FIGO high-risk were also significantly higher than those of patients with FIGO low-risk (25.7% vs. 12.4%, p=0.01 and 13.7% vs. 2.4%, P=0.001, respectively).

Currently, revision of the FIGO scoring system would be needed to allow the early identification of patients developing drug resistance to single-agent chemotherapy and who thus require more intensive chemotherapy, especially those with a FIGO score of 5–6.[7-8] In this study, if the analysis was restricted to the 52 patients with FIGO scores of 5–6, the drug resistance rates of the 17 patients with a clinical choriocarcinoma and 35 with a clinical invasive mole were not significantly different. However, the relapse rate (25.0% vs. 5.7%) was significantly higher in the former group (P=0.001), even though they were initially treated with combination chemotherapy.

Also, the drug resistance and relapse rates of the 35 patients with FIGO 5–6 initially treated with single-agent chemotherapy regimen were 14.3% and 5.7%, respectively, and there were no significant differences compared to patients with FIGO scores of 0–4 and clinical invasive moles (P=0.75 and P= 0.24, respectively).

8.4 CONCLUSION

Both classification systems (the FIGO 2000 risk factor scoring system and the choriocarcinoma risk score table) allow the identification of patients for whom single-agent chemotherapy, or more aggressive chemotherapy, should be recommended. The choriocarcinoma risk score table would be useful for selecting the treatment regimen in patients classified as FIGO 5-6, potentially avoiding treatment failure.

References

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