

# 日本語要約

- ◎ IVa期の膵癌を対象
- ◎ 放射線治療、化学療法、温熱療法、高気圧酸素治療による集学的治療の成果
- ◎ 4者併用の中間生存期間は21ヶ月、2年生存率は42%で、有意に他の治療より良好であった
- ◎ 膵癌は低酸素細胞が多く、温熱療法、高気圧酸素治療を加えた集学的治療は、放射線治療、化学療法の効果を高めるのに有効であると考えられる

# Chemo-radiotherapy plus regional hyperthermia and hyperbaric oxygen therapy for locally advanced pancreatic carcinoma

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# Backgrounds

- To evaluate the efficacy of concurrent chemo-radiotherapy (CRT) plus regional hyperthermia (HT) and hyperbaric oxygen therapy (HBO) for locally advanced primary or post-operative pancreatic carcinoma (LAPC).

# Methods 1

- The patients were 23 males and 17 females, mean age were 63.8 and performance status (PS) was 0-1: 2-3= 23: 17.
- 32 patients were primary disease (stage II: III= 5: 27) and 8 were post-operative local recurrence.
- 10 patients received only CRT (CR group), and 10 patients received regional HT during CRT (CRH group) and 20 received regional HT and HBO during CRT (CRHH group).

# Methods 2

- Chemotherapy
  - > GEM: weekly or biweekly
  - > 400mg/m<sup>2</sup> during radiation therapy
  - > 12 patients were intra-arterially using a subcutaneous port-implantation of an intra-aortic injection adjacent to descending thoracic aorta.
- Hyperthermia
  - > Immediately after Radiation or administration of GEM
  - > No. of session: 24.6±21.5
- Hyperbaric oxygen therapy
  - > Immediately after hyperthermia
  - > No. of session: 28.2±24.6
- Radiation
  - > 50-60Gy/25-34 fractions
  - > Total dose: 58.0±5.0Gy

CR : Chemotherapy/Radiation

CRH : Chemotherapy/Radiation/Hyperthermia

CRHH : Chemotherapy/Radiation/Hyperthermia/Hyper Baric Oxygen

# Table 1: Response rate

Response	No. of cases	Rate
CR	4/40	10%
PR	8/40	20%
SD	28/40	70%
CR+PR	12/40	30%

# Table 2: Distribution of patients and treatment methods

Factor	Group	No. of cases
Age	Under 69 / Over70	25 / 15
PS	0-1 / 2-3	23 / 17
Total dose	Under 60Gy / Over 60Gy	12 / 28
Hyperthermia	Yes / No	30 / 10
HBO	Yes / No	20 / 20
Intra-aortic injection port	Yes / No	12/ 28
Maintenance therapy	Chemo only/ Multidisciplinary therapy	18 / 22

Table 3: Univariate and multivariate analysis for overall survival

Factor	Univariate analysis	Multi-variate analysis	
	P value	P value	hazard ratio
<b>Age</b>	0.30	0.97	1.01
<b>PS</b>	<0.05	<0.05	0.37
<b>Total radiation dose</b>	<0.05	0.95	0.97
<b>Hyperthermia</b>	<0.005	<0.05	0.18
<b>HBO</b>	<0.005	<0.01	0.10
<b>Intra-aortic injection port</b>	<0.01	0.48	0.70
<b>Maintenance therapy</b>	0.06	<0.01	0.09



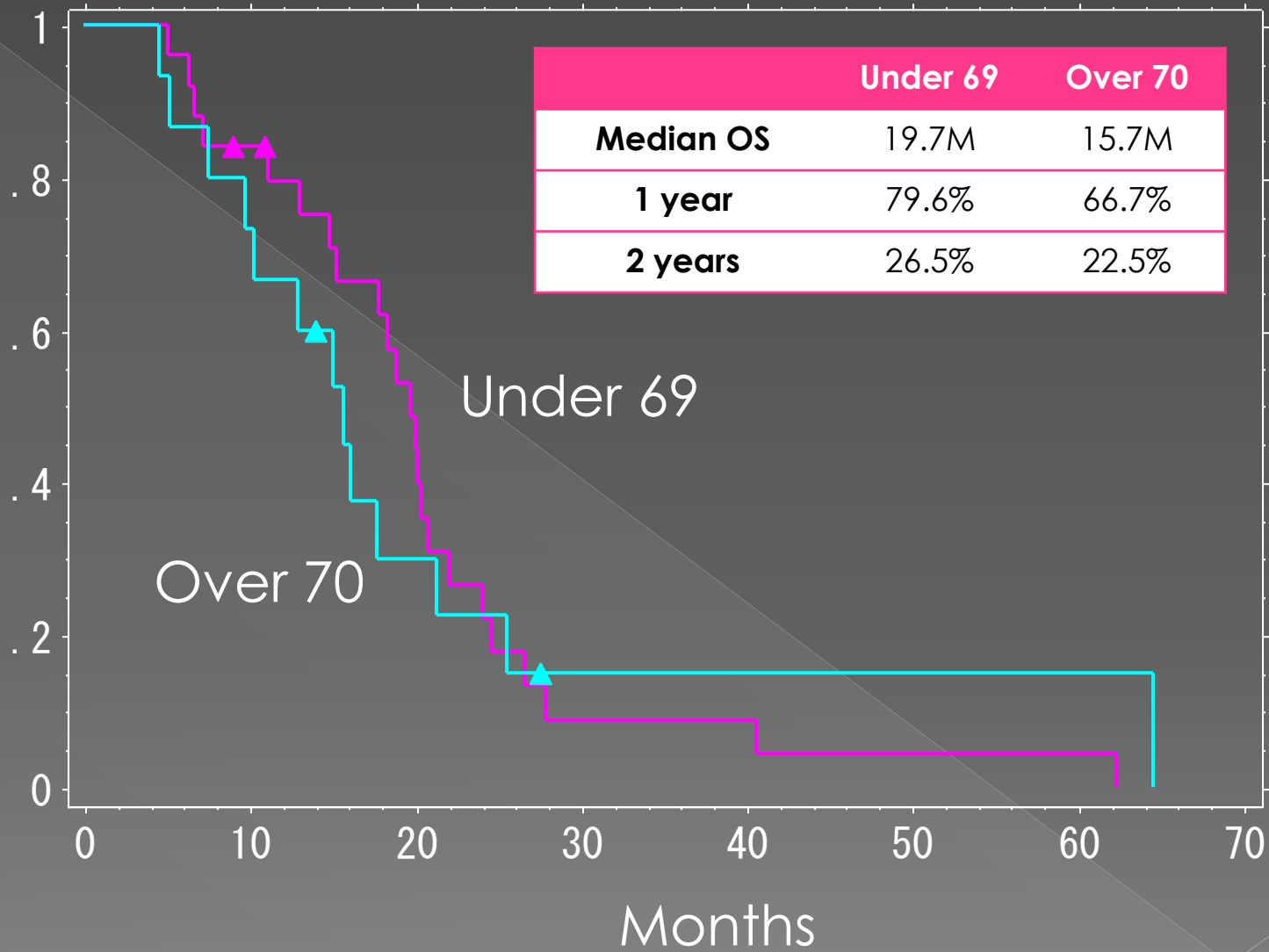


Fig. 1: Overall survival curve by age

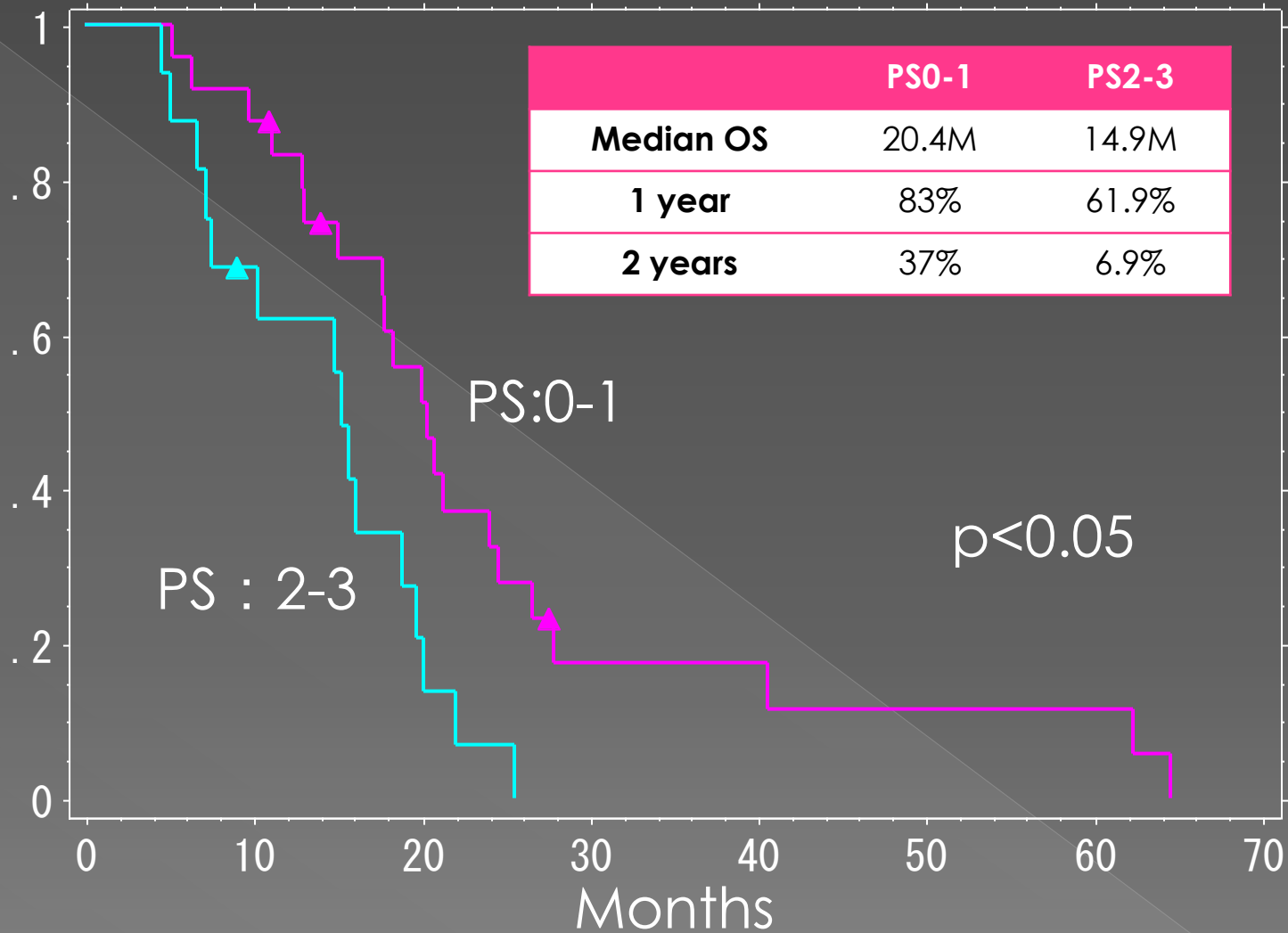


Fig. 2: Overall survival curve by PS

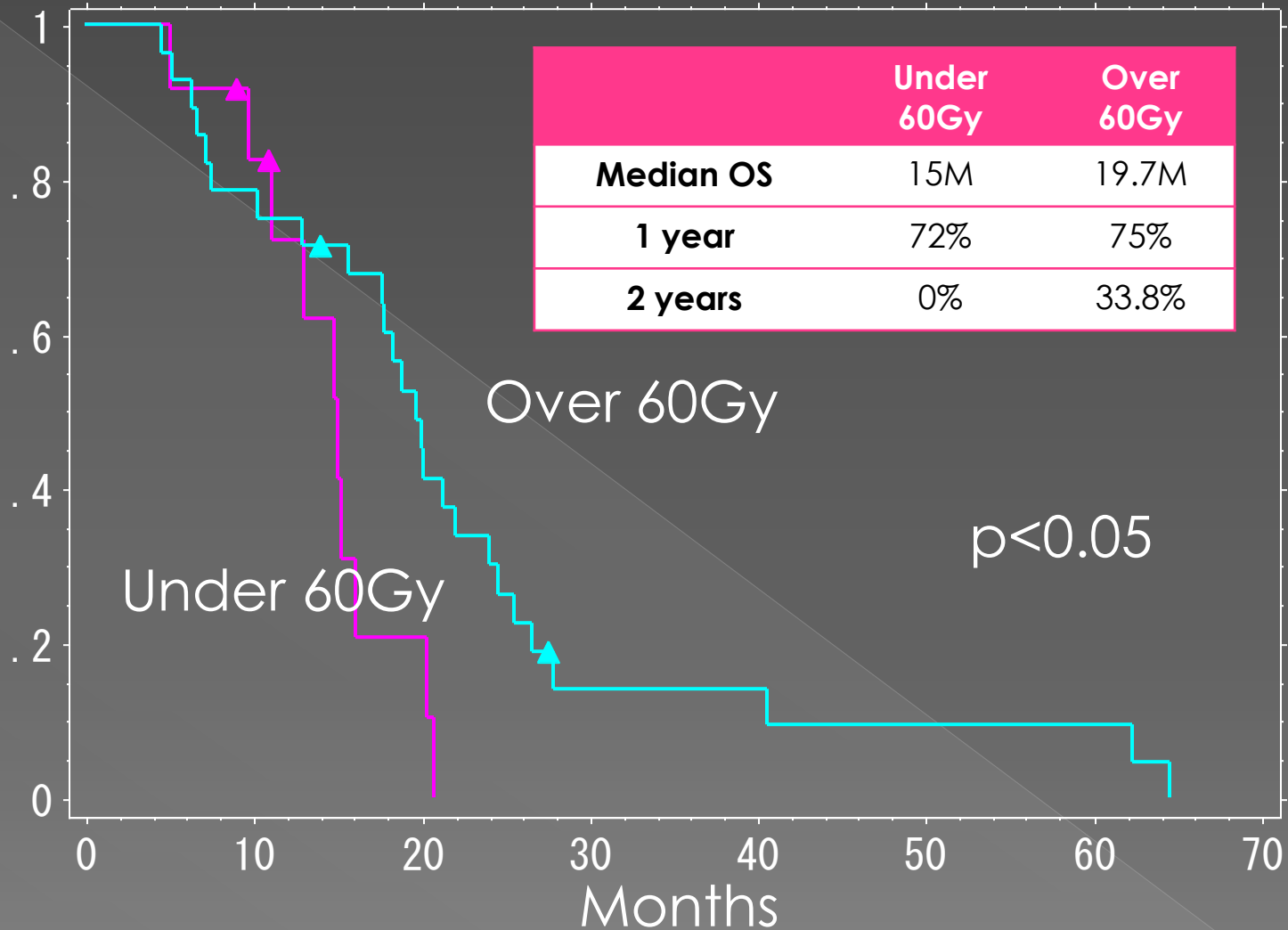


Fig. 3: Overall survival curve by total dose

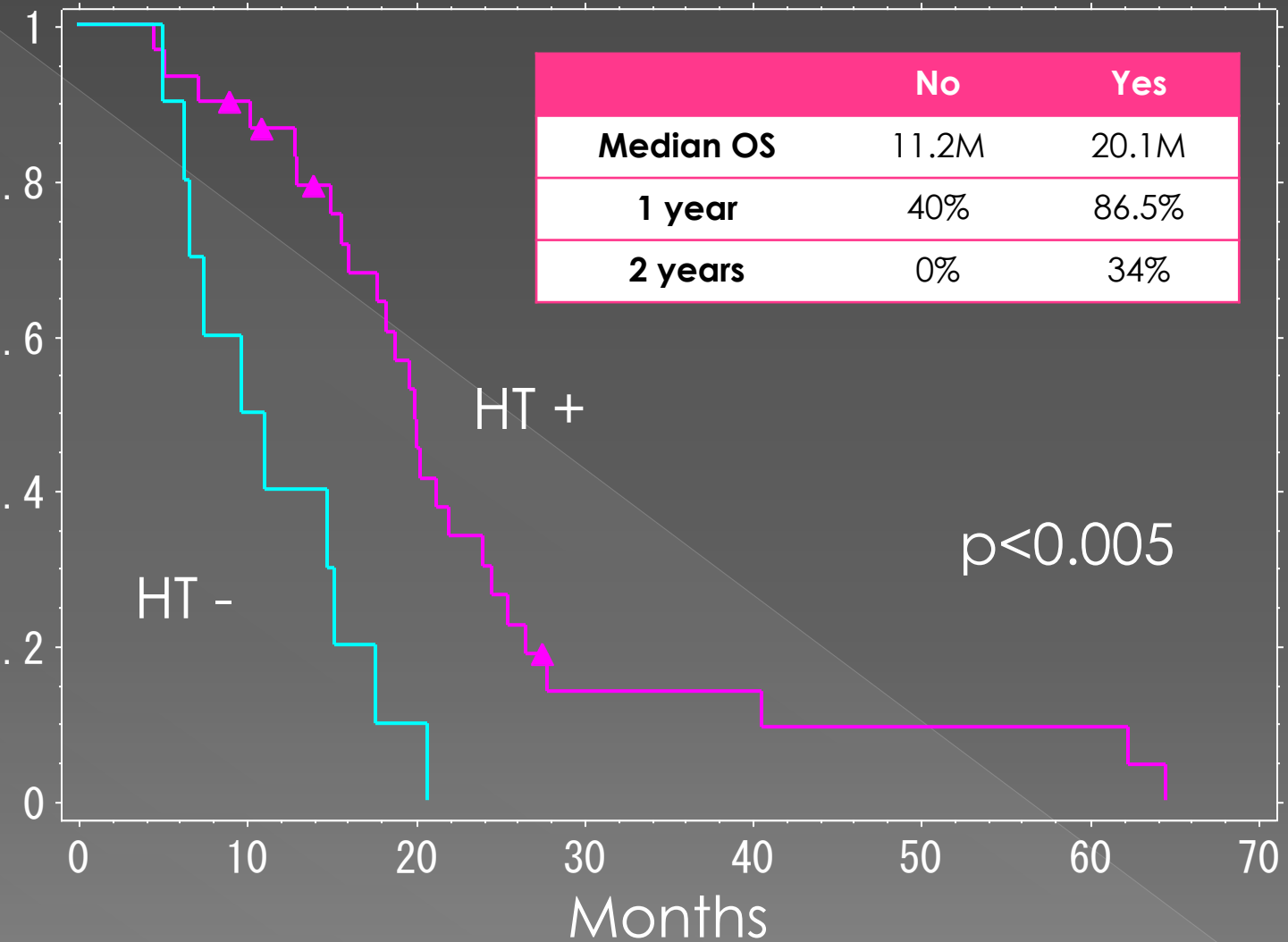


Fig. 4: Overall survival curve with or without HT

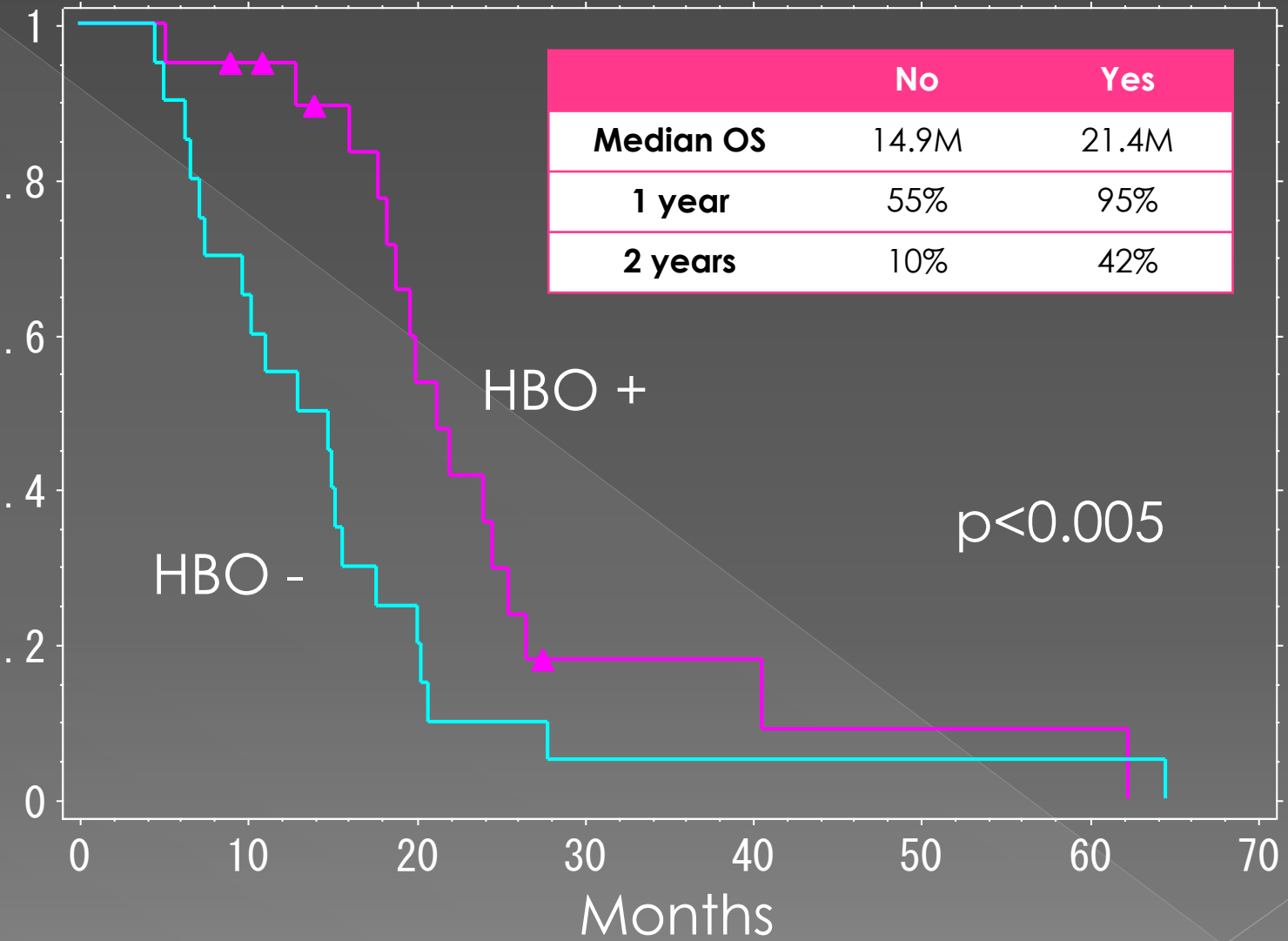


Fig. 5: Overall survival curve with or without HBO

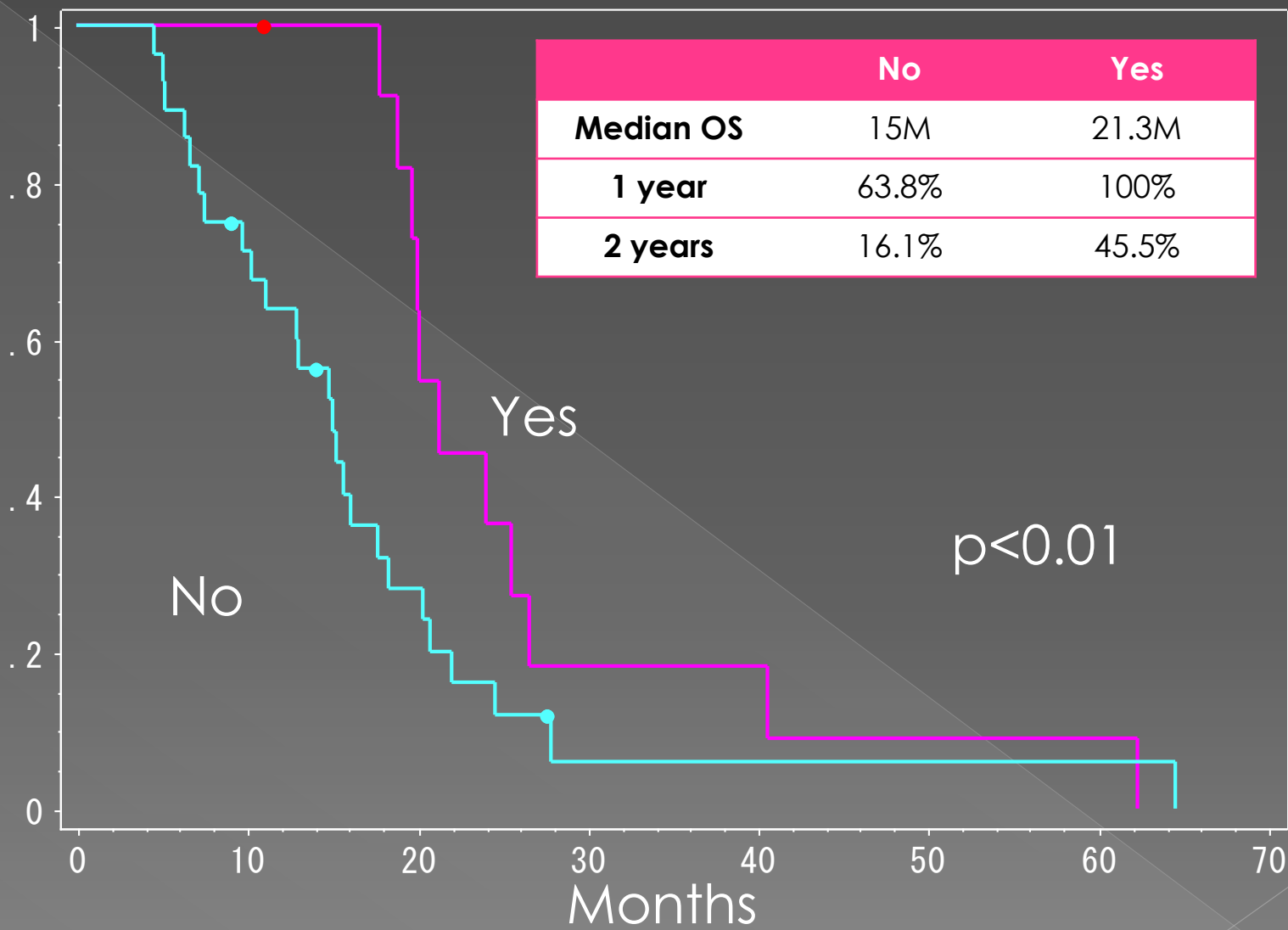


Fig. 6: Overall survival curve by Intra-aortic injection

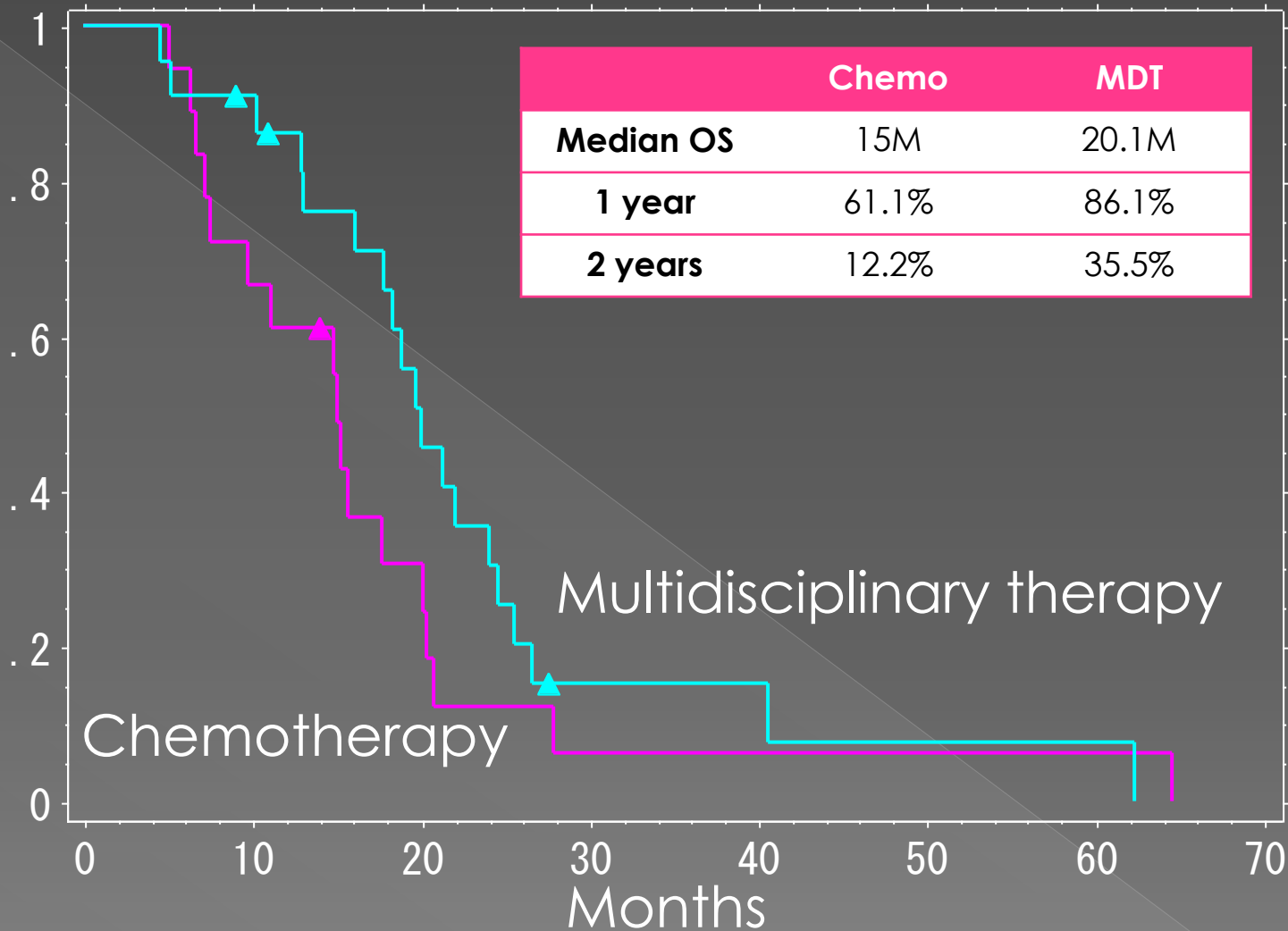


Fig. 7: Overall survival curve by maintenance therapy

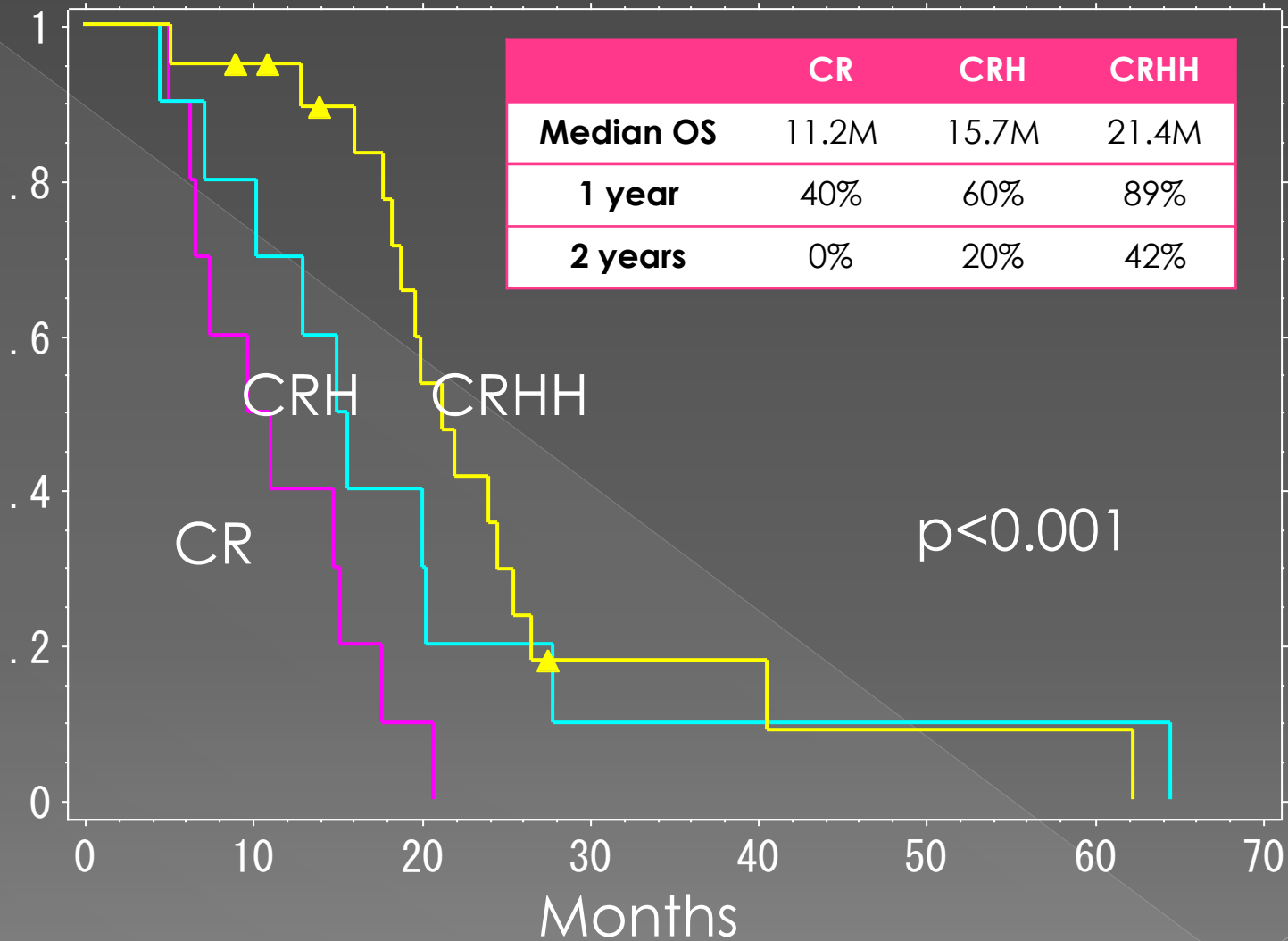


Fig. 8: Overall survival curve by type of combined therapy



# Results

- 70% of patients were SD in local response (Table 1).
- To investigate the effectiveness of combined therapy in CRT for LAPC, statistical analysis for overall survival were done in the factors of Table 2. Table 3 and Fig. 1-7 show the results of univariate and multivariate analysis for overall survival. In both analyses, group of good PS, combination of HT and HBO was significantly better results.
- Fig. 8 showed that median survival time were significantly better for the CRHH group (21.4 months) than for the CRH group (15.7 months) and the CR group (11.2 months).

# Discussion

- LAPC have used chemotherapy (GEM, S-1) and radiotherapy generally. Though sensitivities of chemotherapy and radiotherapy were depended on the proportions of hypoxic cell, pancreatic carcinomas have known the majority of hypoxic cells.
- We combined HT and HBO with CRT, because these were known to send up intra-tumor oxygen concentration in vivo. Better clinical outcome of CRHH group may suggest that CRT with HT and HBO for LAPC has clinical benefit by reoxygenation.

# Conclusion

- Based on these preliminary results, this combined therapy (CRHH) for LAPC may be a feasible and promising regimen, and the results justify further evaluation in a larger number of patients to conclusively confirm its beneficial effect.