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Comparison of radiation doses between hepatic artery infusion chemotherapy and transarterial chemoembolization for liver cancer

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ABSTRACT

Objective: To analyze the radiation dose received by patients during hepatic artery infusion chemotherapy (HAIC) and transarterial chemoembolization (TACE) procedures and the related influencing factors.
Methods: Data of 162 cases in the HAIC group and 230 cases in the TACE group were collected. The included covariates were Age (<45/45–59/≥60 years), BMI levels (underweight/normal weight/obesity), focus Dye of tumor (present/absent), lesion size (<5cm/≥5cm), superselection (present/absent), hepatic vascular variation (present/absent). The endpoints were postoperative dose-area product (DAP), exposure time and Air kerma (AK).
Results: Of all included patients, the HAIC group patients were younger than those in the TACE group ($P = 0.028$). The proportion of patients with large lesions in the HAIC group was higher than the TACE group (45.7% vs. 33.9%, $P = 0.019$). The proportion of patients who had superselection was lower in the HAIC group as compared to the TACE group (61.7% vs. 82.2%, $P < 0.001$). Generally, the HAIC group has lower DAP, exposure time and AK by 36.3% ($P < 0.001$), 38.2% ($P < 0.001$), and 41.3% ($P < 0.001$) than the TACE group, respectively. Linear regression analysis showed the procedure method (HAIC/TACE, $P < 0.001$), type of DSA machine (Pheno/FD20, $P < 0.001$), BMI levels ($P < 0.001$), age ($P = 0.021$), lesion size (<5cm/≥5 cm, $P = 0.031$) significantly correlated with low DAP. In the HAIC group, the type of DSA machine and BMI correlated with the radiation dose, while in the TACE group, the type of DSA machine, BMI, and lesion size correlated with the radiation dose.
Conclusion: Compared with TACE, HAIC enables doctors and patients to receive lower radiation doses. Obese patients in both HAIC and TACE groups increase the radiation exposure in interventional doctors and patients, but large lesions only affect the radiation dose in the TACE procedure.

1. Introduction

Liver cancer is one of the most common cancers in China, the second leading cause of cancer-related deaths in China, and the third leading cause of cancer-related deaths worldwide.[1–3] Vascular interventional treatment of liver cancer has become a clinically safe and effective treatment method, especially for patients who have become unsuitable for surgical resection.[3–5] Research on hepatic vascular interventional therapy has been continuously carried out in recent years. The clinical therapeutic effect of hepatic artery infusion chemotherapy (HAIC) is well known, and long-term continuous arterial infusion of the drug has shown good clinical outcomes.[6–8] However, both transarterial chemoembolization (TACE) and HAIC procedures should be conducted under the guidance of digital subtraction angiography (DSA). During the procedure, the patient receives a heavy dose of radiation, and the surgeon, therefore, must use lead clothing for effective protection. Thus far, the difference in the radiation dose between TACE and HAIC and the related influencing factors are unclear, and this knowledge may aid in improving radiation protection for both doctors and patients.

2. Materials and methods

2.1. Study information and selection criteria

In total, 392 patients who underwent vascular interventional procedures for liver cancer at the Department of Minimally Invasive

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Intervention, Sun Yat-sen University Cancer Center, from November 2019 to April 2020 were chosen, and their medical records were reviewed. The initially selected patients included 336 males and 56 females, aged 21–81 years, with a median age of 54 years. The Sun Yat-sen University Cancer Center Hospital Ethics Committee approved this study. As this study was conducted as a retrospective analysis of routine data, the need for individual informed consent was waived by the ethics committee. All patients signed the informed consent form related to the operation.

The inclusion criteria were as follows:

a) Clinical diagnosis of primary liver cancer;
b) No related surgical contraindications;
c) HAIC and TACE completed successfully.

The exclusion criterion was as follows:

a) Two or more procedures were performed during one treatment session.

2.2. Model parameters

All procedures were performed under the guidance of the angiography system Siemens ARTIS pheno or Philips Allura Xper FD20. In 229 cases that used ARTIS pheno, digital fluoroscopy (DF) and DSA required 7.5 and 5 frames per second, respectively. In 163 cases that used Allura Xper FD20, DF and DSA required 15 and 3 frames per second, respectively. The DF condition for the two machines was Fluo Normal, and the tube voltage, tube current, and other parameters were automatically adjusted. During DSA, the surgeon left the operating room for a short while and entered the control room to watch the real-time radiography video. The image quality of the two models could meet the needs of both TACE and HAIC procedures.

2.3. Intraoperative conditions and radiation dose

All procedures were performed through the femoral artery. The embolization drugs in TACE were delivered to the target tumor using an arterial catheter, and the entire operation was performed in the operating room. In HAIC, when the catheter head reached the target blood vessel, angiographic confirmation was made. After it was confirmed to be correct, the catheter outside the body was directly aseptically bandaged and fixed. Finally, under DSA spot film photography, the patient was transferred to the ward for further arterial infusion treatment after confirmation of the catheter tip position. The interventional doctors and technicians jointly analyzed the intraoperative angiographic images for the following parameters: 1) focus dye of the tumor (present/absent): Present indicated the evident staining and aggregation of the lesion during hepatic DSA, which can be clearly observed. Otherwise, it was considered absent; 2) lesion size (<5 cm/≥5 cm): With the maximum diameter of the focusing dye ≥5 cm as large lesions, non-visualization and <5 cm as small lesions; 3) superselection (present/absent): Present indicated the location of the final catheter tip at the distal end of the bifurcation of the right hepatic artery and the left hepatic artery (right hepatic artery or left hepatic artery). Absent indicated the location of the final catheter tip at the proximal end of the bifurcation of the right hepatic artery and the left hepatic artery (proper hepatic artery); 4) hepatic vascular variation (present/absent): Present indicated the presence of blood-supplying arteries other than the proper hepatic artery in the tumor, including the phrenic artery, superior mesenteric artery, intercostal artery, left gastric artery, gastroduodenal artery, and splenic artery).

Data of the parameters of radiation dosage of the two DSA machines were collected from workstations, and two people recorded the DAP (μGy.m^2), exposure time (s), and AK (mGy) values of each operation. Among them, DAP and exposure time of DF and DSA were referred as DF DAP, DSA DAP, DF time, and DSA time. To discuss the change in DAP between DF and DSA in unit time, we divided DF DAP and DSA DAP by their corresponding DF time and DSA time expressed as DAP/S (μGy.m^2/s).[9]

Table 1
Basic data and intraoperative conditions of patients in the HAIC and TACE groups.

basic situation	HAIC (n = 162)	TACE (n = 230)	χ^2	P
Gender			1.475	0.225
M	143 (88.3%)	193 (83.9%)		
F	19 (11.7%)	37 (16.1%)		
Age (years)			7.183	0.028
<45	50 (30.9%)	44 (19.1%)		
45–59	64 (39.5%)	107 (46.5%)		
≥60	48 (29.6%)	79 (34.3%)		
BMI (kg/m^2)			1.179	0.555
<18.5	14 (8.6%)	17 (7.4%)		
18.5–24.9	121 (74.7%)	165 (71.7%)		
≥25	27 (16.7%)	48 (20.9%)		
focus Dye of tumor			0.136	0.712
absent	55 (34%)	74 (32.2%)		
present	107 (66%)	156 (67.8%)		
lesion size (cm)			5.543	0.019
<5 or absent	88 (54.3%)	152 (66.1%)		
≥5	74 (45.7%)	78 (33.9%)		
superselection			20.51	<0.001
absent	62 (38.3%)	41 (17.8%)		
Present	100 (61.7%)	189 (82.2%)		
hepatic vascular variation			2.071	0.150
absent	144 (88.9%)	214 (93.0%)		
present	18 (11.1%)	16 (7.0%)		
DSA machine			2.348	0.125
Pheno	102 (63%)	127 (55.2%)		
FD20	60 (37%)	103 (44.8%)		

The calculation method is as follows:

$$DAP = DF\ DAP + DSA\ DAP$$

$$exposure\ time = DF\ time + DSA\ time$$

$$DF\ DAP/S = DF\ DAP/DF\ time$$

$$DSA\ DAP/S = DSA\ DAP/DSA\ time$$

All data were recorded twice by two independent nurses involved in the research and checked by the researcher to ensure consistency.

2.4. Statistical analysis

Statistical analysis was performed using SPSS Statistics, version 23.0. Categorical variables are expressed as counts and percentages, and continuous variables are expressed as medians and quartiles. The Wilcoxon rank-sum test was used to compare the radiation dose differences between HAIC and TACE. The Chi-square test was used to compare categorical variables between groups. Multifactor linear regression analysis was used to analyze the factors influencing radiation dose and to separately analyze the radiation dose factors that affect HAIC and TACE, with all relevant factors computed as categorical variables. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Study information and intraoperative conditions

Data on age, sex, body mass index (BMI), focus dye of the tumor, lesion size, superselection, hepatic vascular variation, and DSA model of patients for HAIC and TACE were statistically analyzed (Table 1). Compared with the TACE group, the HAIC group had more young

Table 2
Radiation dose of HAIC and TACE.

Radiation dose parameters	HAIC (n = 162)	TACE(n = 230)	P
DAP (μGy.m^2)	5561.7 (3285.1, 8975.0)	8734.1 (4944.8, 13968.8)	<0.001
exposure time (s)	357 (192, 564.5)	578 (354.8936)	<0.001
AK (mGy)	133.5 (75.2, 214.9)	227.4 (148, 369.3)	<0.001
DF DAP (μGy.m^2)	1266.1 (572.6, 2803.3)	1471.1 (731.9, 3072.7)	0.148
DF time(s)	340 (174, 534)	548.5 (322, 904)	<0.001
DSA DAP (μGy.m^2)	3831.7 (2475.9, 6052.6)	6231.5 (3711.8, 10752.8)	<0.001
DSA time(s)	18 (16, 24)	30(18,42)	<0.001
DF DAP/s (μGy.m^2/s)	4.16 (2.47, 6.89)	2.76 (1.51, 5.19)	<0.001
DSA DAP/s (μGy.m^2/s)	196.42 (138.1, 298.4)	215 (145, 309.24)	0.516

Abbreviations: DAP (dose-area product); AK (Air kerma); DF DSA (digital fluoroscopy DAP); DSA DAP (digital subtraction angiography DAP).

patients (30.9% vs. 19.1%, P = 0.028), a higher proportion of large lesions (≥5 cm) (45.7% vs. 33.9%, P = 0.019), and a lower proportion of superselection (61.7% vs. 82.2%, P < 0.001).

3.2. Comparison of the radiation dose between HAIC and TACE

In terms of radiation dose in the HAIC group, the median DAP was 5561.7 μGy m^2 (quartile: 3285.1, 8975.0), the median exposure time was 357 s (quartile: 192, 564.5), and the median AK was 133.5 mGy (quartile: 75.2, 214.9). The corresponding values in the TACE group were 8734.1 μGy m^2 (quartile: 4944.8, 13968.8), 578 s (quartile: 354.8936), and 227.4 mGy (quartile: 148, 369.3). Compared with TACE, in the HAIC group, DAP was reduced by 36.3% (P < 0.001), the exposure time was reduced by 38.2% (P < 0.001), and AK was reduced by 41.3% (P < 0.001) (Table 2, Fig. 1).

As for the relative radiation doses of DF and DSA in HAIC and TACE, the median values of DF DAP in the HAIC and TACE groups were 1266.1 μGy m^2 (quartile: 572.6, 2803.3) and 1471.1 μGy m^2 (quartiles: 731.9, 3072.7), respectively. The median DF times in the HAIC and TACE groups were 340 s (quartile: 174,534) and 548.5 s (quartile: 322, 904), respectively. The median values of DF DAP per second in the HAIC and TACE groups were 4.16 μGy m^2/s (quartile: 2.47, 6.89) and 2.76 μGy m^2/s (quartile: 1.51, 5.19), respectively. The median values of DSA DAP in the HAIC and TACE groups were 3831.7 μGy m^2 (quartile: 2475.9, 6052.6) and 6231.5 μGy m^2 (quartile: 3711.8, 10752.8), respectively; the corresponding median DSA times were 18 s (quartile: 16, 24) and 30 s (quartile: 18, 42); the median values of DSA DAP per second in the HAIC and TACE groups were 196.42 μGy m^2/s (quartile: 138.1, 298.4) and 215 μGy m^2/s (quartile: 145, 309.24). (Table 2, Figs. 2–4).

3.3. Factors affecting patient radiation dose

Linear regression analysis showed that procedure method (HAIC or TACE, P < 0.001), type of DSA machine (pheno/FD20, P < 0.001), BMI (P < 0.001), age (P = 0.021), and lesion size (<5 cm/≥5 cm, P = 0.031) significantly correlated with low DAP (Table 3). In the HAIC subgroup, type of DSA machine and BMI significantly correlated with radiation dose, whereas in the TACE subgroup, type of DSA machine, BMI, and lesion size significantly correlated with radiation dose (Table 4).

4. Discussion

This study showed that the DAP of HAIC was reduced by 36.3% compared with that of TACE, which is a great advantage. In further analysis of the influence of fluoroscopy and angiography on DAP, DAP of angiography in HAIC was found to be reduced by 38.5% when compared

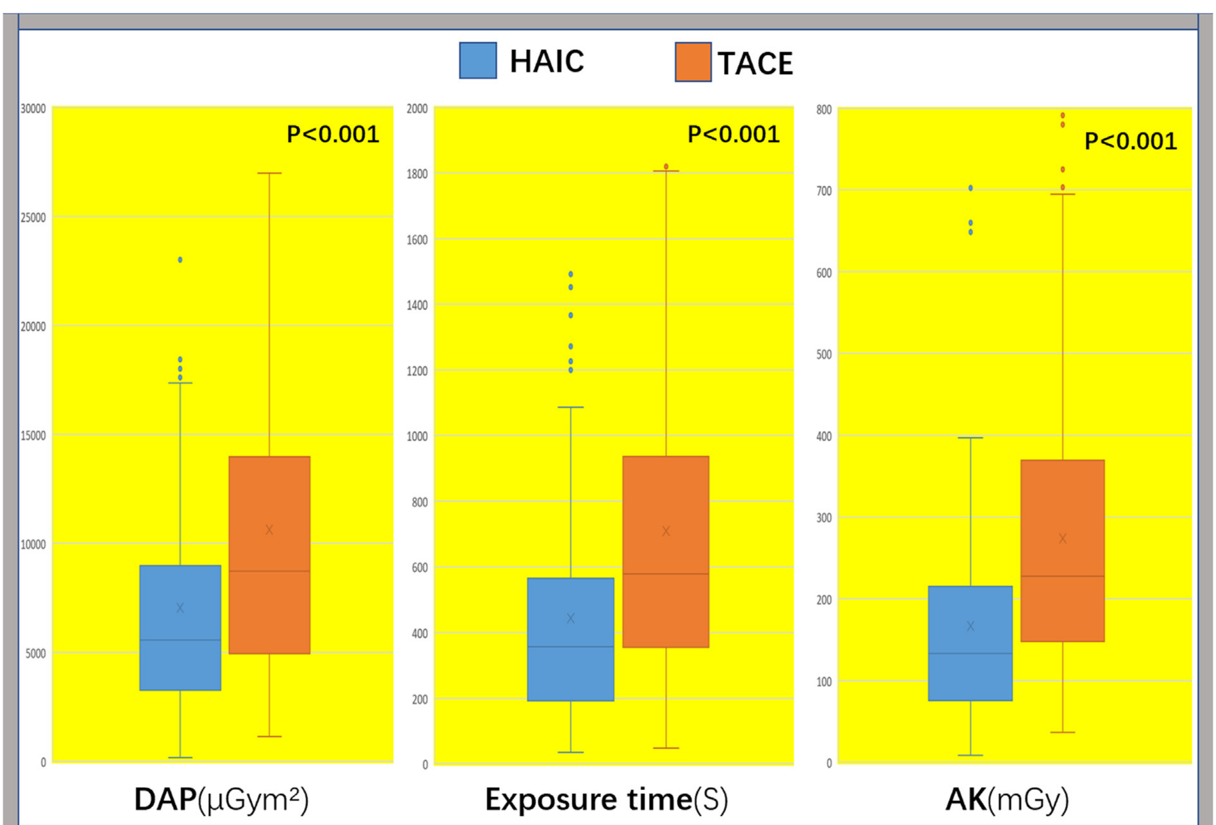

Fig. 1. Data distribution of DLP, exposure time and AK of HAIC and TACE.

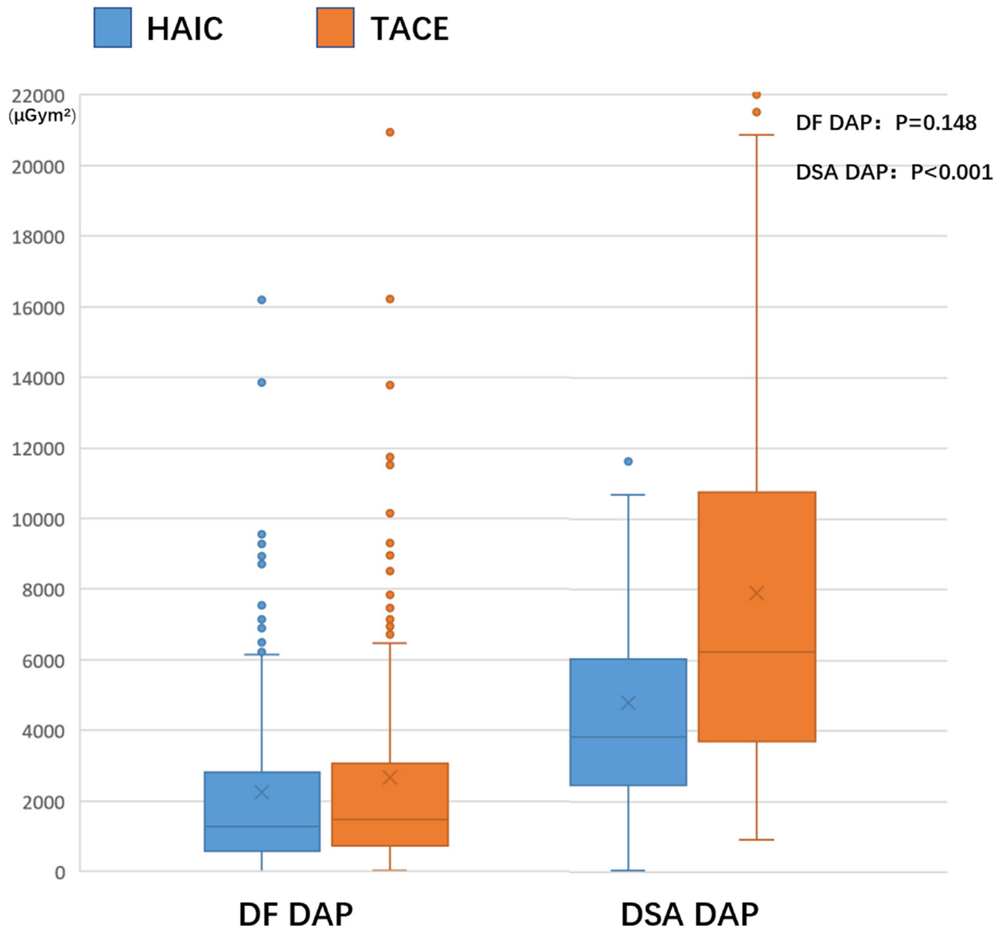

Fig. 2. The specific distribution of digital fluoroscopy DAP (DF DAP) and digital subtraction angiography DAP (DSA DAP) in HAIC and TACE.

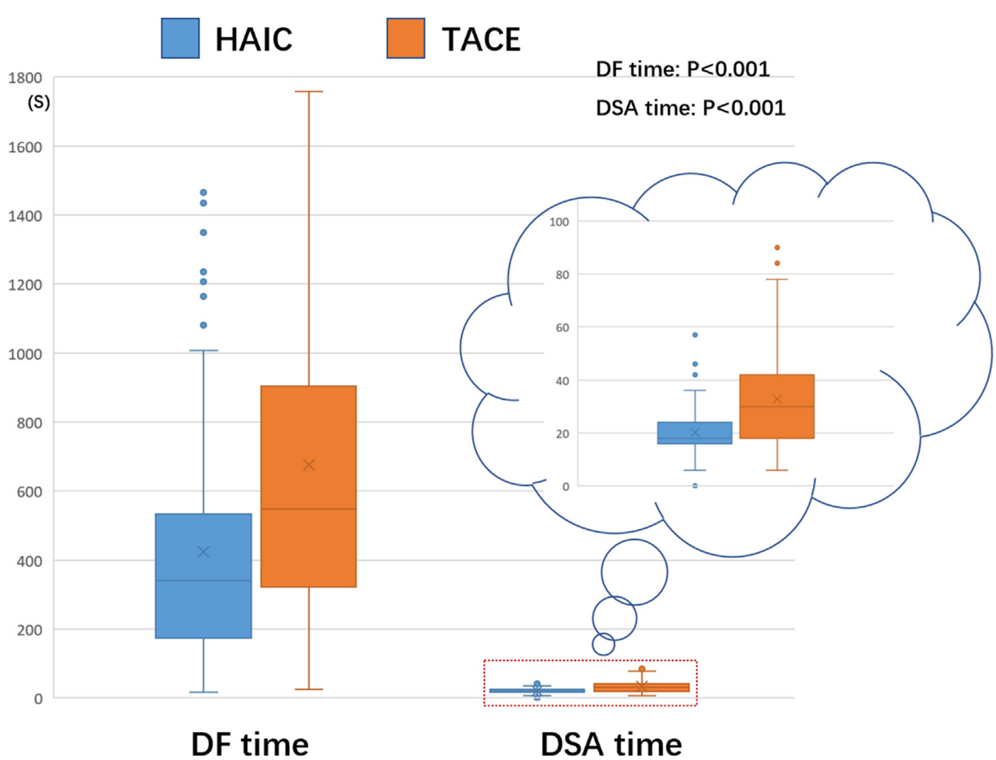

Fig. 3. The specific distribution of digital fluoroscopy time (DF time) and digital subtraction angiography time (DSA time) in HAIC and TACE.

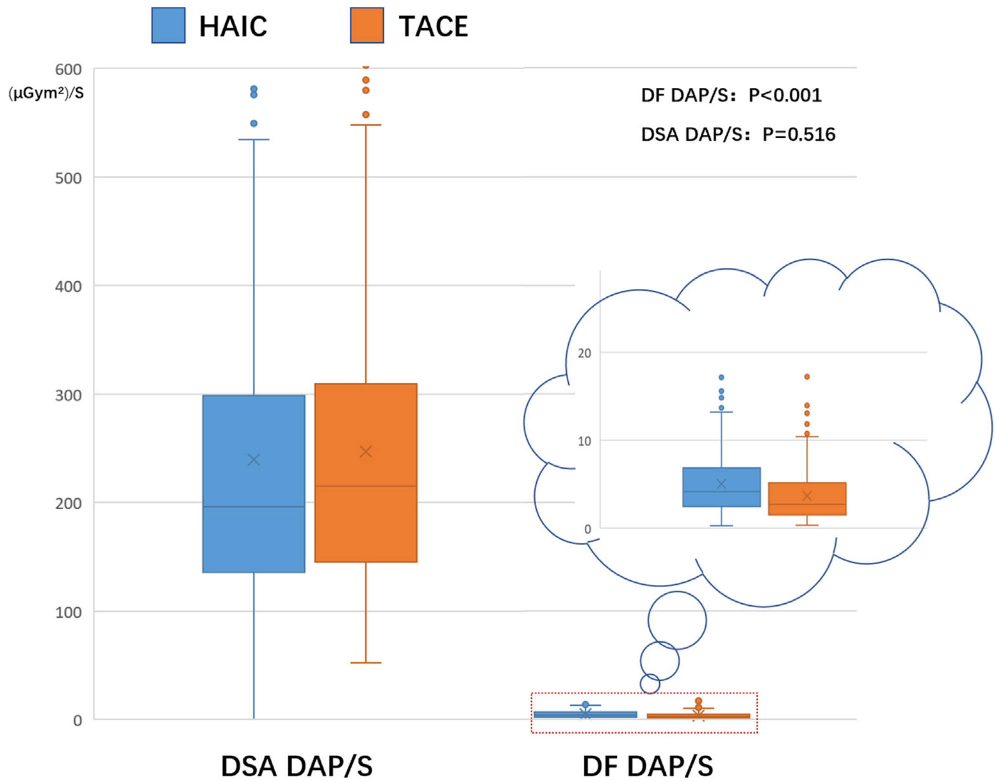

Fig. 4. The specific distributions of DF DAP and DSA DAP per unit time in HAIC and TACE.

Table 3
Radiation dose multi-factor linear regression analysis table.

factor	Unstandardised coefficients		Standardised coefficients beta	t	P	95.0% confidence interval for B	
	B	Std. error				Lower	Upper
DSA machine (Pheno/FD20)	6508.249	590.567	.444	11.020	<0.001	5347.118	7669.380
BMI(<18.5/18.5–24.9/≥25 kg/m^2)	4662.659	566.240	.328	8.234	<0.001	3549.359	5775.959
procedure method (HAIC/TACE)	2828.600	589.945	.193	4.795	<0.001	1668.693	3988.506
Age(<45/45–59/≥60 year)	896.602	387.990	.093	2.311	0.021	133.764	1659.440
lesion size (<5cm/≥5 cm)	1302.825	602.270	.088	2.163	0.031	118.685	2486.966

Table 4
Multivariate linear regression analysis of HAIC and TACE.

factor	Unstandardised coefficients		Standardised coefficients beta	t	P	95.0% confidence interval for B	
	B	Std. error				Lower	Upper
HAIC							
DSA machine (Pheno/FD20)	6218.873	760.838	.516	8.174	<0.001	4716.220	7721.526
BMI(<18.5/18.5–24.9/≥25 kg/m^2)	3669.723	739.802	.313	4.960	<0.001	2208.618	5130.829
TACE							
DSA machine (Pheno/FD20)	6568.717	851.037	.423	7.718	<0.001	4891.735	8245.698
BMI(<18.5/18.5–24.9/≥25 kg/m^2)	5555.563	803.831	.370	6.911	<0.001	3971.601	7139.526
lesion size (<5cm/≥5 cm)	2134.055	895.525	.131	2.383	0.018	369.408	3898.701

with that in TACE ($P < 0.001$), but in fluoroscopy DAP, the difference between HAIC and TACE was not significant ($P = 0.148$). Our results suggest that the reduction in the radiation dose of HAIC in comparison with TACE is mainly due to the reduction in the DAP of angiography. This study is the first to compare the radiation doses of HAIC and TACE in the treatment of liver cancer.

In this study, the median DAP of angiography during TACE and HAIC was 6232 μGy m^2 and 3832 μGy m^2, respectively, which accounted for nearly 70% of the total median DAP (8734 μGy m^2 and 5562 μGy m^2, respectively). TACE treatment requires higher angiography times than HAIC treatment, which is consistent with the finding that TACE treatment requires more refined superselection and additional post-embolization angiography evaluation than HAIC treatment in clinical practice. We found that in fluoroscopic DAP, the difference between HAIC and TACE was not statistically significant. However, it is strange that at the time of fluoroscopy, HAIC, in comparison with TACE, decreased by 38%, and the difference was also statistically significant ($P < 0.001$). Regarding the surgical procedures of HAIC and TACE, it is not difficult for us to understand that during fluoroscopy, doctors routinely reduce the FOV to reduce the radiation dose. Although the FOV is reduced in HAIC, this occurs much less frequently than in TACE. Because embolic agents are part of the medications in TACE, it is necessary to monitor the flow of embolic agents in real time during injections. The larger the lesion, the slower the process. Doctors tend to reduce the FOV as much as possible to reduce the degree of radiation. Therefore, in fluoroscopy, fluoroscopy time in HAIC, when compared with that in TACE, decreased by 38% ($P < 0.001$), and DAP in HAIC decreased by only 13.9% ($P = 0.148$). This finding is consistent with the results of Wei Chao et al.,[10] who studied the influence of FOV on radiation dose.

We analyzed the factors influencing DAP in liver interventional surgery and found that the type of surgical method (HAIC or TACE), different machines, BMI, age, and lesion size have an impact on DAP. In the study by Javor et al.,[11] the upgraded flat panel detector could reduce the DAP of TACE from a median value of 395.8 Gy cm^2 to 132.9 Gy cm^2. Therefore, the influence of different machines on the radiation dose is very large. The impact of BMI on DAP is mainly reflected in terms of the changes in the voltage and current of the X-ray tube, as shown in the study of cardiac catheterization, which was conducted by Osei et al.[12] BMI also has an impact on the radiation dose. As BMI increases, the voltage of the X-ray tube also increases, which eventually leads to a corresponding increase in the radiation dose. The effect of age on DAP lies mainly in the difference in blood vessels. As age increases, the elasticity of the arterial wall decreases, and atherosclerosis and related functions of the abdominal aortic wall are impaired.[13] This often increases the difficulty of the operation, which leads to an increase in DAP. The impact of lesion size on DAP lies mainly in exposure time. Large lesions often need to be injected with more drugs. In TACE, the injection of embolic drugs needs to be observed in real time. As the use of drugs increases, the exposure time also increases. Therefore, the DAP also increases accordingly. However, in the multivariate analysis of HAIC and TACE, the size of the lesion affected only the DAP of TACE and was not related to the DAP of HAIC. The findings of factors affecting the radiation dose can provide a detailed reference for interventional doctors and enhance their own radiation protection abilities.

The shortcomings of this study are the lack of FOV-related data during fluoroscopy of HAIC and TACE in the analysis of radiation dose differences; moreover, and the fluoroscopy and angiography results were inconsistent. This can be explained only by the intraoperative procedure and related literature. In addition, this study may not be comprehensive in reporting relevant factors that affect the radiation dose. There are still many factors that affect DAP that cannot be controlled for. In summary, the patient's exposure time and radiation dose during HAIC were significantly lower than those during TACE, and the exposure time of interventional doctors was significantly reduced. However, the difference between the radiation dose exposure among interventional doctors in HAIC and TACE is not obvious, and we have shown that the interventional doctor's control of FOV in HAIC needs to be further optimized. The present study can provide a basis for future studies in terms of enhancing radiation protection abilities of interventional doctors and reducing the radiation dose exposure in patients and interventional doctors.

Declaration of competing interest

The authors declare no conflict of interest.

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