Tolerability of endobiliary photodynamic therapy in non-surgical Klatskin tumour patients

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Aims and objectives

Cholangiocarcinoma is the second most common primary malignant tumor of the liver. Klatskin tumor or hilar cholangiocarcinoma represents more than 50% of all biliary tract cholangiocarcinomas [1]. The natura history of Klatskin tumors is dramatic. The median survival without interventions reaches three months, and it may be prolonged by drainage from four to ten months [2]. The patients die mainly due to jaundice, cholangitis, liver failure, complications of portal hypertension and cachexia. The majority of patients are not surgical candidates, so other therapies are required toincrease their survival and improve the quality of life (Fig. 1 on page 3).

Endobiliary photodynamic therapy (EPDT) - is a binary tumor destruction procedure implying more or less specific accumulation of intravenously injected agent named photosensitizer by proliferative cells and inflammatory tissue following by intraductal laser irradiation (Fig. 2 on page 3 , Fig. 3 on page 4). According to the literature the treatment of cholangiocarcinoma with endobiliary PDT is associated with an increased survival benefit, an improved biliary drainage, and a better quality of life (Fig. 4 on page 5). Varying intraductal light delivery equipment, irradiation regimen and light doses as well different photosensitizers using for EPDT may impact its safety. Identification of factors influencing EPDT tolerability in non-surgical Klatskin tumor patients is the purpose of the paper.

Images for this section:

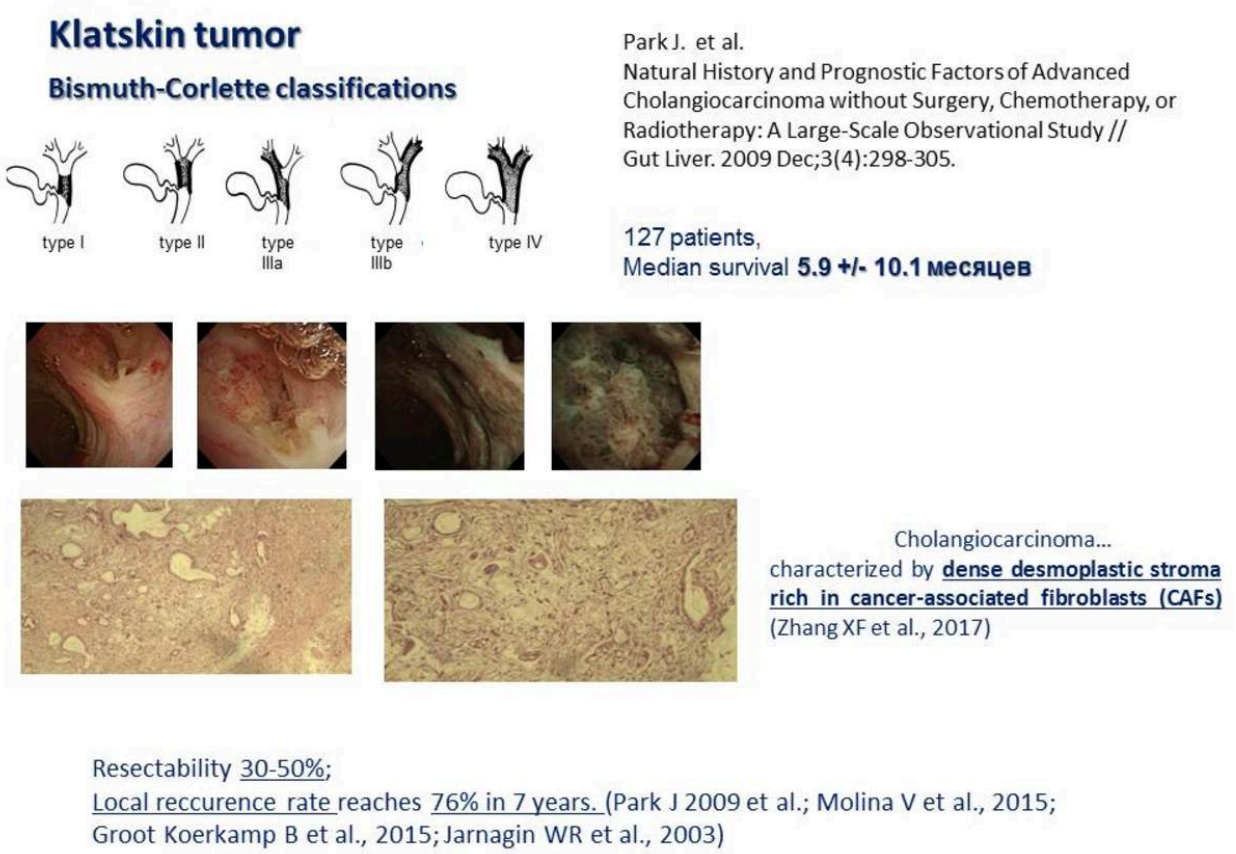
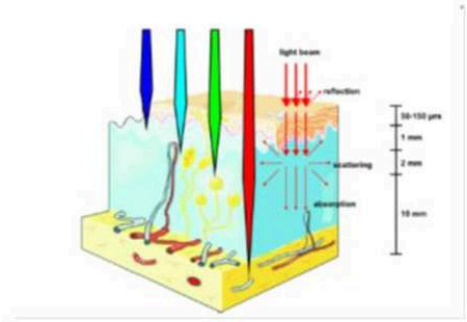
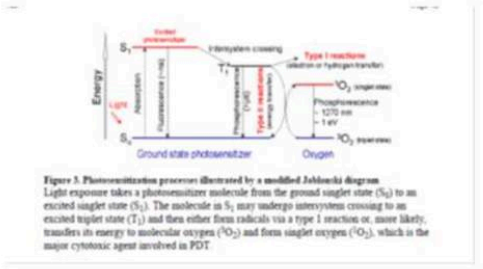


Fig. 1

Photodynamic therapy: basic principles





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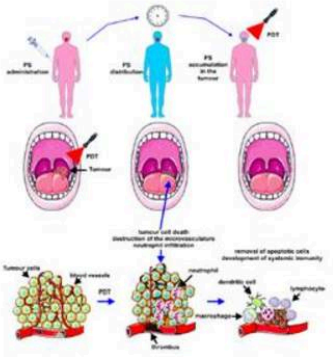

Fig. 2

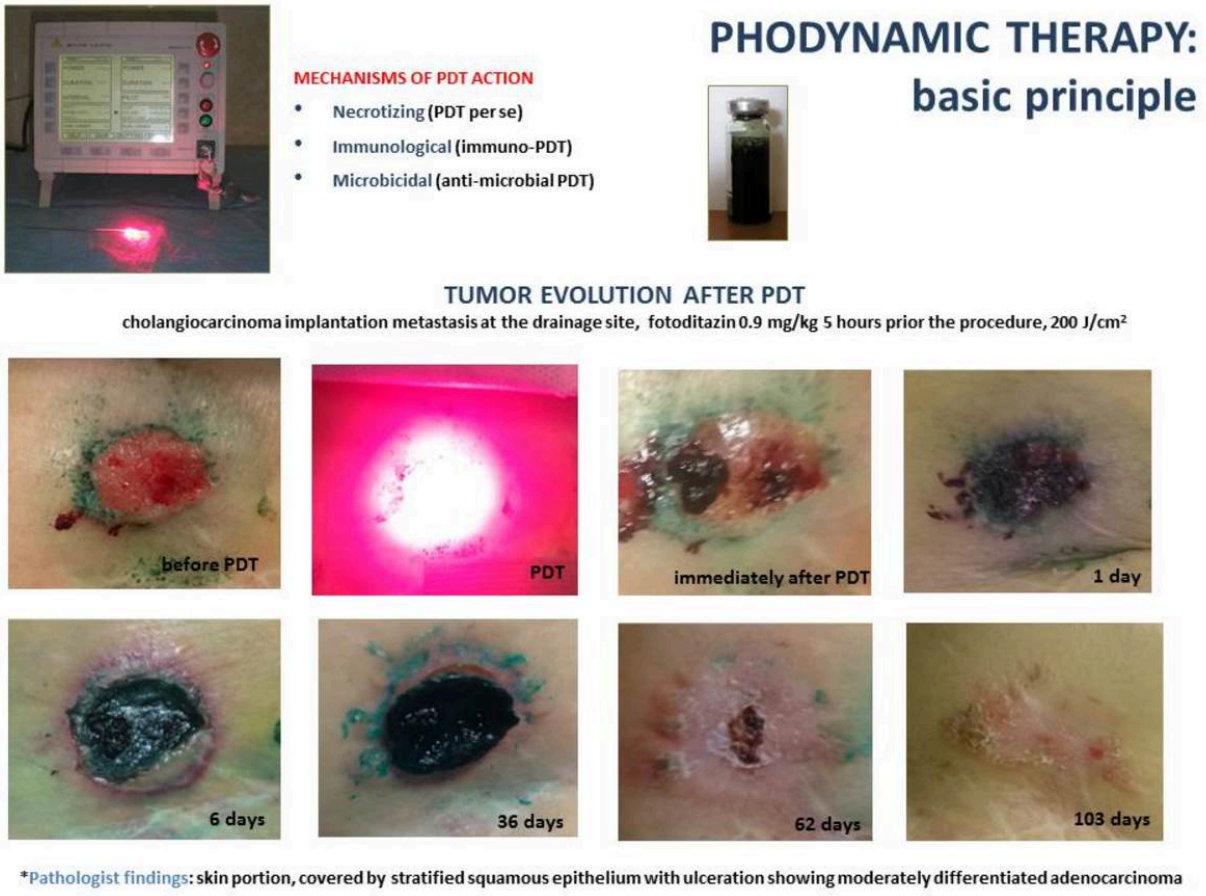

Fig. 3

Эффективность ФДТ: данные литературы

Author	Year	Number of patients	Median survival	Results
Ortner M.E. et al. (Centre Hospitalier Universitaire Vaudois, Switzerland)	2003	19 – stenting only	98 дней	research discontinued for ethical reasons
		20 – stenting + PDT	493 дня	
Zoepf T. et al. (University Hospital Essen, Germany)	2005	11 – biliary drainage only	7 мес	PDT has the potential to result in a changeover of current palliative treatment of BDC
		11 – biliary drainage + PDT	21 мес	
Yi Lu et. al. (Shanghai Jiaotong University School of Medicine, China). A meta-analysis of 7 trials.	2015	266 – stenting + PDT 336 – stenting only		The palliative treatment of cholangiocarcinoma, with photodynamic therapy, is associated with an increased survival benefit, an improved biliary drainage, and a better quality of life.
Harsha Moole,et. al (University of Illinois College of Medicine,United States). A systematic review and meta-analysis	2017	402		Survival period in PDT and BS groups were 413.04 d (95%CI: 349.54-476.54) and 183.41 (95%CI: 136.81-230.02) respectively.

Fig. 4

Methods and materials

The intraprocedural adverse events of 159 EPDT's performed in 62 biopsy confirmed non-surgical Klatskin tumor patients in a ten-year period were studied. The endobiliary light delivery was fulfilled though the previously inserted percutaneous transhepatic biliary drainage channels by mean of a 600 μm in diameter optical fiber with a 2 to 6 cm diffuser tip after prior 2 to 5 hours i.v. injection of chlorin photosensitizers (Fig. 5 on page 8). Intraprocedural adverse events included pain, hemodynamic disorders, shaking chill, nausea and vomiting. They were distributed into 3 grades: 1 - no or requiring medication only; 2 - requiring fluence rate reduction; 3 - requiring procedure cessation (Fig. 6 on page 9). Their dependence on total dose (range 64.6-3240 J), fluence rate (range 19,1 - 288 mW/cm2), power density (range 14,5-206,3 J/cm2), diffuser tip length (2,3,5,6 cm) , number of channels (range 1-4), photoexposure time (range 3-240 min), photosensitizing drug (Photolon, Fotoditazin, Radahlorin) and its dosage (0.6-2.0 mg/kg) was analyzed (Fig. 5 on page 8).

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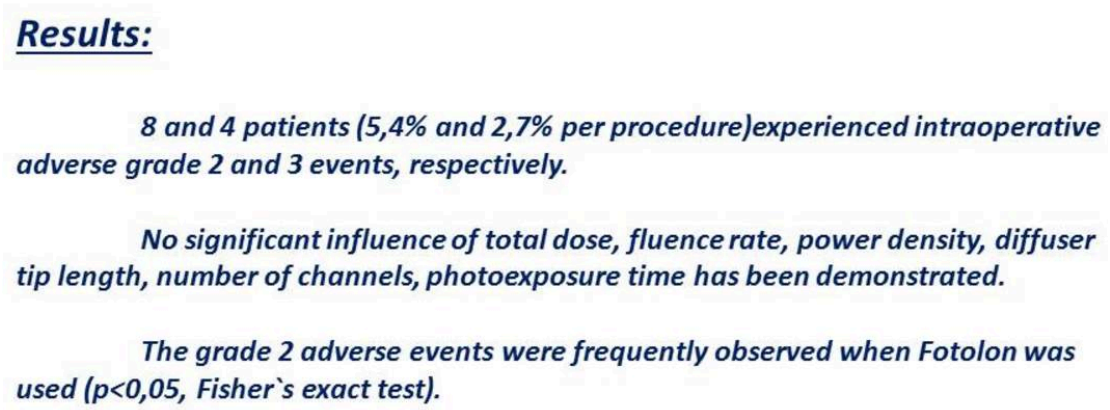

Fig. 7

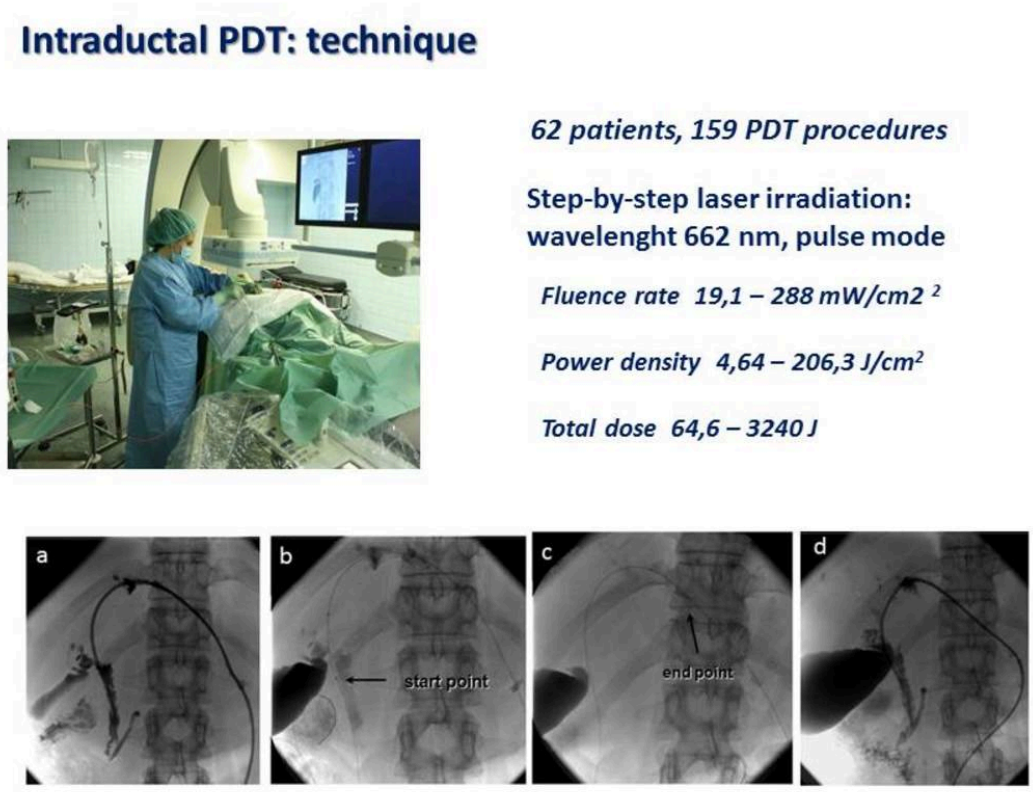

Fig. 5

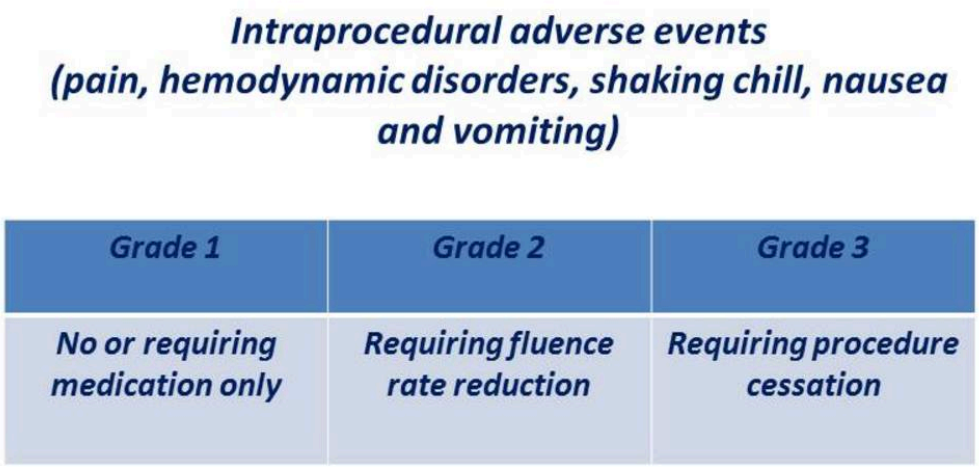

Fig. 6

Results

Eight and 4 patients (5,4% and 2,7% per procedure)experienced intraoperative adverse events grade 2 and 3 events, respectively. No significant influence of total dose, fluence rate, power density, diffuser tip length, number of channels, photoexposure time has been demonstrated. The grade 2 adverse events were frequently observed when Fotolon was used ($p<0,05$, Fisher`s exact test), but further investigation are required due to small number of cases (Fig. 7 on page 12).

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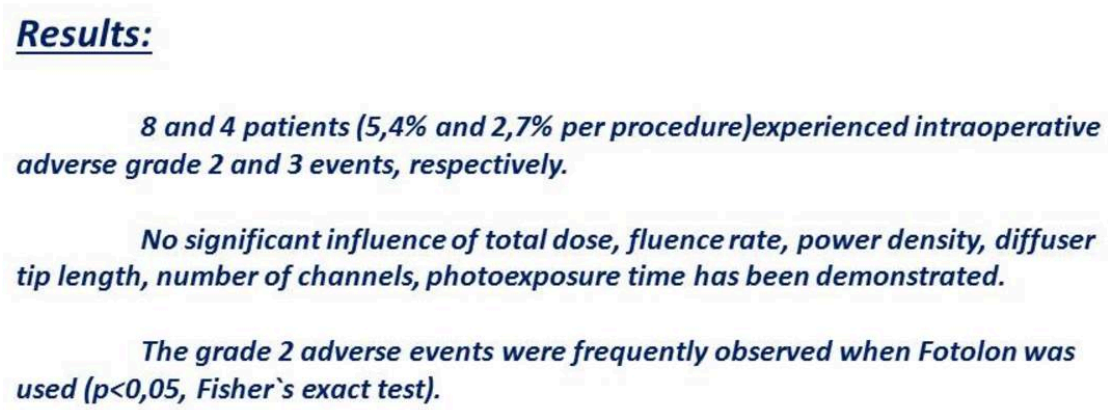

Fig. 7

Conclusion

Endobiliary PDT is effective and well tolerated procedure. Small number of intraprocedural adverse events hampers identification of factors influencing EPDT tolerability.

References

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