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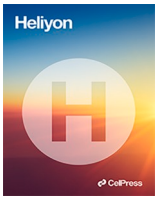

Research article

Body fat percentage vs body mass index in estimating basal cell carcinoma

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ABSTRACT

Background: The role of body mass index (BMI) in basal cell carcinoma (BCC) risk remains controversial, and limited information is available regarding the relationship between other physical measurements and BCC. Several recent studies have found a positive effect of adiposity on improved survival when obesity was determined solely by BMI (the "obesity paradox"). We hypothesize that body fat percentage (BFP) may serve as a more sensitive risk factor for BCC than BMI.

Methods: The study conducted a retrospective analysis of clinical data from two distinct centers in China. Individual patient-level data were obtained from medical record reviews spanning January 1, 2015, to December 31, 2022. Associations with outcomes were analyzed using univariate and stratified analyses and assessed using multiple logistic regression with adjustment for confounding factors. Additionally, we performed a meta-analysis to further test the observations in our study.

Results: A total of 337 patients, ranging in age from 50 to 91 years, with a mean age of 66.88 (standard deviation 10.16), were included. We observed no significant association between BMI and BCC after adjusting for confounders (OR: 0.71, 95 % CI: 0.36–1.40, $P = 0.3186$). There was also no convincing effect in a meta-analysis (n = 158,741) (OR: 0.99, 95 % CI: 0.93–1.06, $P = 0.8$). Furthermore, BFP was found to be associated with BCC (OR: 2.64, 95 % CI: 1.17–5.97, $P = 0.0196$), supported by strong clinical evidence.

Conclusions: Our study supports the hypothesis that BFP is superior to BMI in assessing BCC risk. Multiple logistic regression analyses, coupled with meta-analysis, provided robust evidence that BFP is a sensitive risk factor for BCC, while BMI appears unrelated to risk. According to these findings, routine healthcare practices could benefit from utilizing BFP measurements. The reduction of body fat percentage in low-fat diets may be beneficial for adjuvant treatment of BCC.

1. Introduction

Basal cell carcinoma (BCC) is one of the most common skin malignancies [1,2]. Early manifestations typically include pearl-like

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local prominences with peripheral telangiectasia. Late symptoms, however, are diverse, leading to potential misdiagnosis or missed diagnoses. Basal cell carcinoma is a low-grade malignant tumor characterized by slow growth and rare metastasis. If left untreated in a timely manner, BCC can progress and deteriorate, ultimately causing irreversible damage or even death [3]. The understanding of obesity as a risk factor for several diseases largely relies on anthropometric indices such as body mass index (BMI) [4,5]. However, BMI is an indirect measure of adiposity that fails to distinguish between fat and muscle [6,7]. Some individuals considered healthy due to a normal BMI might actually have cardiometabolic diseases, collectively termed metabolic obesity in normal weight [8]. Meanwhile, it is known as obesity paradox in oncology that cancer patients with elevated BMI have lower mortality rates and better cancer-specific survival rates than those with normal BMI [9].

Retrospective studies report conflicting data regarding the roles of BMI in BCC, and clinical efficacy data vary significantly between different institutions, likely because the relationship between body fat and BCC is not taken into account and only limited information is available on this issue. Using BMI as a measure of adiposity is imperfect because it does not distinguish fat from lean mass. There is evidence that excess fat mass may be detrimental to health, whereas lean body mass may be beneficial [10,11].

Therefore, we hypothesized that body fat percentage (BFP) serves as a more sensitive risk factor for BCC. To test our hypothesis, we collected disease-related data from two distinct institutions and reviewed all relevant published studies to analyze the association between BMI and BCC from the compiled data. The purpose of this study was to determine what effect BMI and BFP had on the prognosis of BCC and provide support for BCC risk evaluation in guiding physical examinations.

2. Materials and methods

2.1. Multicenter study using logistic regression analysis

To achieve our study objectives, we employed a retrospective case-control design. The inclusion criteria consisted of individuals aged 50 and older, without previous history or special medications that could affect the results. BCC was confirmed by final pathological findings. A total of 148 BCC patients and 189 age-matched healthy controls were included in our analysis between January 1, 2015, and December 31, 2022, in the Nanjing Drum Tower Hospital and the Affiliated Hospital of Qingdao University. Before surgery, participants underwent basic examinations and had their results recorded in case files to ensure surgical safety. Clinical data included age, sex, nation, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), BMI, BFP, smoking status, alcohol consumption, UV exposure, and living area. Table S1 summarizes the clinical characteristics of patients and prevalence data.

BMI was calculated by dividing weight in kilograms by the square of height in meters. BFP was measured using the equation verified by Deurenberg: $BF\% = (1.2 \times BMI) + (0.23 \times age) - 5.4 - (10.8 \times S)$ (0 = women, 1 = men) [12,13]. Obesity was defined by the World Health Organization Asian reference as BMI $\geq$25 kg/m^2 [14]. The ranges of dyslipidemia were as follows: TC $\geq$ 6.2 mmol/L, LDL-C $\geq$ 4.1 mmol/L, TG $\geq$ 2.3 mmol/L, and HDL-C $\leq$ 1.0 mmol/L [15].

2.2. Systematic review and meta-analysis

The study systematically searched the PubMed and Embase databases to identify relevant studies. All retrieved publications were manually screened for additional relevant citations in their references. Study population characteristics, adjustment variables, health outcomes, and study quality were included in the extracted data. We included participants who met specific criteria, and data were collected using standardized data collection forms. Our analysis covered characteristics such as the first author's name, study title, publication year, country, age and sex of participants, number of participants, BMI measurement methods, BMI categories with corresponding odds ratios (ORs) and 95 % confidence intervals (CIs), and analyses adjusted for confounding factors. Three authors (Zheng Dong, Zhenyu Chen, and Qian Tan) independently searched the literature, selected studies, and extracted data, with any discrepancies resolved by consensus. Rather than scoring the methodological quality of the included studies, we investigated whether different survey methods and population characteristics influenced summary risk estimates to obtain more precise quality indicators.

The following studies were eligible for inclusion: (1) Studies with case-control, cohort, or nested case-control designs; (2) BMI as the main exposure of interest (in kg/m^2); (3) For continuous BMI, relative risks (RRs) with 95 % CIs were calculated for BCC or its subtypes. When multiple publications were reported on the same study, the one with the largest number of BCCs was analyzed. (4) All study subjects were from the general population.

2.3. Statistical analysis

The data are presented as means and standard deviations for continuous variables and as frequencies (percentages) for categorical variables. A multivariate logistic regression analysis was used to assess the effect of BMI on BCC. By adjusting for age, sex, BMI, and lipid levels, logistic regression was used to estimate ORs and 95 % CIs for primary outcomes. A statistical significance threshold of 0.05 was set for two-tailed *P*-values in all analyses. Data analysis was performed using R and Empower (R). Review Manager (version 5.3) was used for the meta-analysis. For the purposes of this systematic review, we categorized outcome variables based on the Japan Society for the Study of Obesity definition of obesity as a BMI $\geq$25 kg/m^2. BMI and BCC correlations were calculated using the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [16]. When BMI was reported in its continuous form, linear regression models were used for all continuous outcomes (ORs). The method of generalized least squares, as described by Greenland and Longnecker, was used to estimate outcomes for categorical BMI [17], which requires the ORs, CIs, and data for at least two categories

of cases and participants. If the adjusted ORs and CIs were not available, we derived data from the respective unadjusted parameters. The study was conducted using a random-effects model. An analysis of publication bias was conducted using the funnel plot method. A result was considered statistically significant if the *P*-value was less than 0.05. Fig. 3 was drawn by Figdraw (www.figdraw.com, ID: RPIWS4d4ad).

3. Results

3.1. Baseline characteristics

The baseline characteristics of BCC and control subjects are presented in Table S1. Satisfactory internal homogeneity was observed among the participants in the two groups. Therefore, the data from both groups were combined for analysis. A total of 148 patients (79 males/69 females; mean age of 68.15 years) were diagnosed with BCC as the experimental group, and there were 189 individuals in the control group (90 males/99 females; mean age of 65.88 years). When comparing clinical features, potential risk factors, including age, living areas, TC, HDL-C, and TG levels, showed statistically significant differences between BCC cases and matched controls. However, no statistically significant differences were found among potential risk factors for sex, smoking, alcohol consumption, UV exposure, weight, height, race, and TC.

4. BMI in relation to BCC

In single-factor analysis, we observed a grouping effect in potential risk factors. Comparing baseline characteristics between participants with and without BCC, participants with BCC tended to have higher levels of BMI, BFP, TC, HDL-C, and TG (Table S2). Table 1 shows the BMI-adjusted ORs and 95 % CI for BCC related to the study factors. Overall, a stratified analysis of the association between BMI and BCC was conducted based on covariates such as age, sex, weight, height, and lipid profiles, showing that the pathogenic effects varied based on the grouping (OR $>$ 1). In multiple logistic regression analyses, the relationship between BMI and BCC is summarized in Table 2. We did not observe an association between BMI and BCC (OR: 1.17, 95 % CI: 0.76–1.81, $P = 0.4776$).

Table 1
Association between BMI and BCC according to baseline characteristics.

Subgroup	n	OR, 95%CI	*P*-value
Age Tertile (y)			
50-61	99	2.05 (0.87, 4.84)	0.1030
61-71	119	0.94 (0.45, 1.95)	0.8607
71-91	119	0.91 (0.44, 1.88)	0.8020
Sex			
Male	169	0.88 (0.48, 1.60)	0.6664
Female	168	1.54 (0.82, 2.90)	0.1825
Height Tertile (cm)			
140-159	89	0.83 (0.34, 2.06)	0.6925
159-170	135	1.68 (0.84, 3.38)	0.1413
170-213	113	0.96 (0.46, 2.02)	0.9144
Weight Tertile (kg)			
42-60	95	0.43 (0.05, 4.03)	0.4610
60-71	125	0.96 (0.44, 2.08)	0.9119
71-115	117	1.33 (0.44, 4.02)	0.6095
BFP Tertile (%)			
23.77–35.56	112	0.62 (0.26, 1.50)	0.2918
35.56–42.02	112	1.47 (0.68, 3.17)	0.3248
42.02–59.17	113	1.35 (0.63, 2.90)	0.4343
TC Tertile (mmol/l)			
1.99–4.85	111	1.14 (0.50, 2.62)	0.7534
4.85–5.43	112	2.57 (1.15, 5.75)	0.0211
5.43–9.14	114	0.40 (0.18, 0.88)	0.0220
HDL-C Tertile (mmol/l)			
0.70–1.52	112	1.56 (0.74, 3.32)	0.2443
1.52–2.60	112	2.01 (0.81, 5.00)	0.1343
2.60–8.60	113	0.32 (0.15, 0.71)	0.0048
LDL-C Tertile (mmol/l)			
0.74–2.99	111	0.82 (0.36, 1.86)	0.6318
2.99–3.37	112	3.87 (1.74, 8.60)	0.0009
3.37–6.79	114	0.65 (0.30, 1.37)	0.2562
TG Tertile (mmol/l)			
0.13–1.17	112	0.93 (0.39, 2.21)	0.8623
1.17-1.45	107	0.98 (0.42, 2.24)	0.9525
1.45–6.92	118	0.84 (0.39, 1.80)	0.6548

TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; BMI, body mass index; BFP, body fat percentage; OR, odds ratio; CI, confidence interval.

The result remained stable after adjusting for other confounders (OR: 0.71, 95 % CI: 0.36–1.40, $P = 0.3186$).

A total of 56 articles were identified in the literature review. Ultimately, five articles were included in our study [18–22]. Fig. 1 shows detailed information for each article. This research comprised 154,170 participants and 4571 BCC cases. According to the Newcastle-Ottawa Scale, Fig. 2A summarizes the risk of bias. Our meta-analysis results were consistent with this finding after excluding the highly selective cohort studies. There was no statistically significant difference among the two groups (OR: 0.99, 95 % CI: 0.93–1.06, $P = 0.8$). A summary of these data, along with their publication bias, is shown in Fig. 2B.

4.1. BFP in relation to BCC

Subsequent stratified analysis revealed the association between BFP and BCC in covariates (Table 3). There were some disparities in outcomes when stratified. The results of the multiple models are shown in Table 4. We found that BFP may be a risk factor for BCC after adjusting for confounders (OR: 1.06, 95 % CI: 1.01–1.11, $P = 0.0187$). BCC was more likely to occur in participants with a higher BFP (OR: 2.64, 95 % CI: 1.17–5.97, $P = 0.0196$). According to the BFP risk stratification analysis, the risk of high levels of BFP was significantly increased compared to low and medium levels of BFP. We found that the risk of BCC was significantly elevated at a BFP greater than 42.02, and this result was statistically significant (OR: 2.64, $P = 0.0196$).

5. Discussion

Skin basal cell carcinoma is one of the common malignant tumors of the skin, mainly derived from the epidermis or appendages [23,24]. Current research suggests that BCC occurs with ultraviolet light, smoking, excess alcohol consumption, ionizing radiation, arsenic, radiotherapy, local chronic inflammation, burns, and immunosuppressive factors, but the exact pathogenesis of BCC remains to be further explored. In this study, we found that BFP was a more sensitive risk factor for BCC. In previous research, BMI has been shown to be useful for assessing some specific disease risks, but it may not be the most suitable parameter biologically [25,26]. Obesity and overweight defined by BMI have been widely used and reported. Despite this, BMI may not be a sensitive indicator of certain diseases' risk due to the confusion of the "obesity paradox," i.e., obese people usually show lower prevalence and mortality [27–30]. Meanwhile, BMI has certain limitations in distinguishing between lean muscle and body fat. The correlation between BCC and BMI remains controversial. Some studies have shown obesity to be a protective factor against BCC. This is difficult to interpret the positive association between BCC and serum lipids. In comparison, BFP displayed a more exciting potential role for cancer and cardiovascular diseases, which reveals the obesity paradox using BMI measurement. Since their clinical significance as risk factors was less well investigated, the current results have made considerable progress in the existing research, especially for guiding healthcare in practice and the early risk evaluation of some diseases.

In retrospective case-control studies, BCC showed no apparent correlation with BMI after adjustment for potential confounders, and our meta-analysis results were consistent with this finding after excluding the highly selective cohort studies. Some reasons could account for this finding. BMI does not precisely distinguish between lean muscle and fat mass, which means that people with the same BMI may have different fat distributions and levels [31]. BMI is inaccurate to assess among the following factors, which are also confounding factors for BCC. Sarcopenia is also present in patients with chronic wasting diseases. Most smokers have a lower weight and a higher waist-to-hip ratio. Meanwhile, there were also differences in the lean and fat distribution of individuals with extreme height and very muscular. Few people have the habit of sunbathing due to the living habits and living environment in Asia. In our clinical work, we found that most patients paid attention to sun protection in their daily lives. In addition, we also found that higher BFP was associated with a higher risk of BCC (OR: 2.64, 95 % CI: 1.17–5.97, $P = 0.0196$). When the BFP was greater than 42.02, the risk of BCC was significantly increased. There is no consensus on the critical point of BFP in WHO [32]. It provides support for the study of BFP. Abnormal or excessive fat accumulation may increase the risk of developing BCC. The mechanism of association between BFP and BCC may be related to functional mutations of Patched (PTCH) or Smoothened (SMO), and the aberrant activation of the hedgehog (Hh) signaling pathway as well as lipid metabolism can stimulate hedgehog signaling [1,33,34] (Fig. 3). In contrast to the result for BMI, we found that higher BFP was associated with BCC. Indeed, BFP more accurately reflects body composition than BMI. The accumulation of adipose tissue has a dysregulated effect on the hedgehog signaling pathway [35]. Simultaneously, the occurrence of BCC is closely related to the abnormal activation of the Hh pathway, and the disorder of the Hh pathway also leads to obesity and an increase in lipid profiles [36,37]. Another possible explanation is that fat accumulation may be associated with chronic systemic inflammation [38].

The advantage of our study is that we examined the role of BFP in BCC for the first time. And we found that BMI may not perform

Table 2
Association between potential risk factors and BCC according to baseline characteristics.

	Non-adjusted		Adjust	
	OR, 95 % CI	*P*-value	OR, 95 % CI	*P*-value
<25 kg/m^2	1.0		1.0	
≥ 25 kg/m^2	1.17 (0.76, 1.81)	0.4776	0.71 (0.36, 1.40)	0.3186

TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; OR, odds ratio; CI, confidence interval.
Adjust model adjust for: sex; age (y); nation; area; weight (kg); LDL-C (mmol/l); HDL-C(mmol/l); TC (mmol/l); TG (mmol/l).

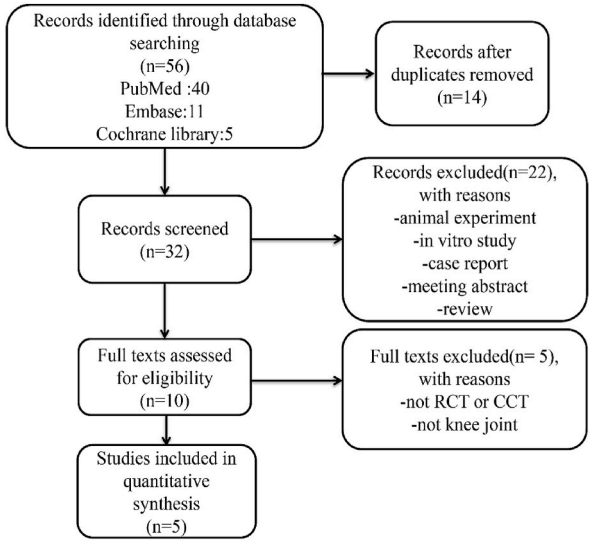

Fig. 1. Articles identified and evaluated during the review process.

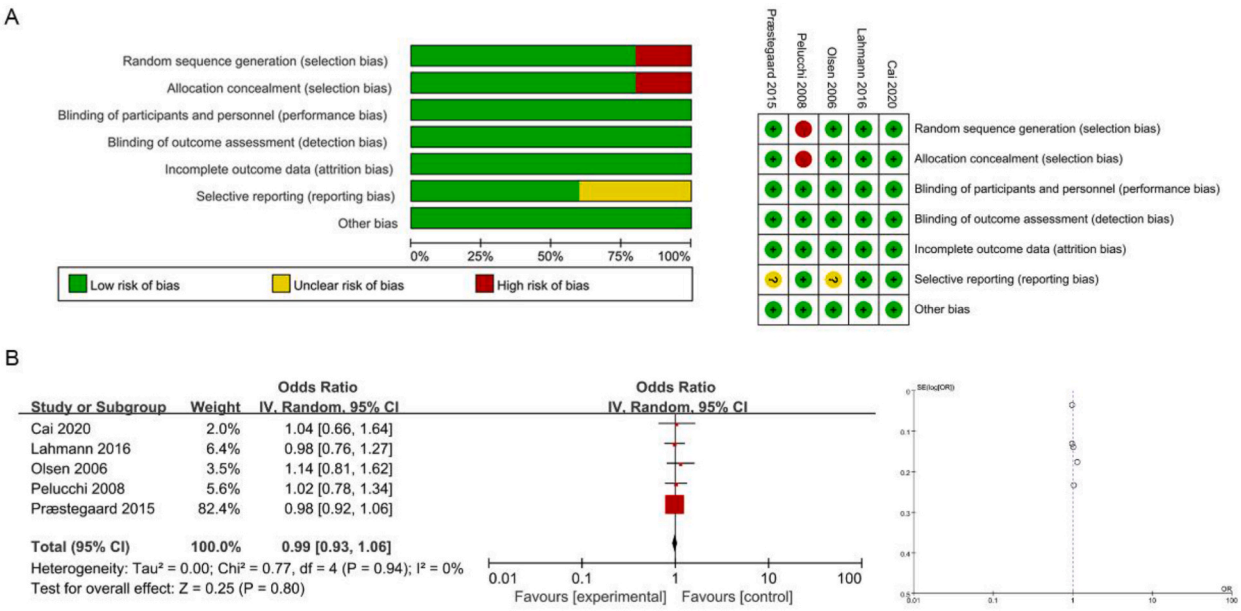

Fig. 2. (A) The risk of bias according to the Newcastle-Ottawa Scale and summarized.(B) Forest plot and Begg's funnel plot showing content of BMI as a risk factor in BCC and publication bias.

optimally as a risk factor for BCC. Therefore, we provided critical evidence for the application of BFP. It has potential utility and practicality, just like BMI. Certainly, this method also has some limitations. The calculation of BFP was based on the equation, which may not be as accurate as special instrument measurements. These valuable findings should be tested in larger sample sizes and under more conditions.

In conclusion, our findings indicate the potential value of BFP in BCC assessment than the commonly used BMI. BMI showed poor prognostic performance in BCC compared with its performance in most situations. These findings indicated that BFP could be a more individualized predictor of disease risk. This study provided evidence for the application of BFP in routine health examinations due to its effectiveness and convenience. The detection of BFP comes at a relatively low cost compared to more refined techniques such as MRI. BFP may be used to roughly assess body fat percentage and identify patients at high risk of underlying BCC during daily physical examinations, combined with family history can further provide corresponding preventive measures and precautions.

Table 3
Association between BFP and BCC according to baseline characteristics.

Subgroup	n	OR, 95 % CI	*P*-value
Age Tertile (y)			
50-61	99	1.02 (0.96, 1.09)	0.4553
61-71	119	1.00 (0.95, 1.06)	0.8827
71-91	119	0.98 (0.93, 1.03)	0.4330
Sex			
Male	169	1.03 (0.96, 1.10)	0.3782
Female	168	1.06 (1.00, 1.13)	0.0511
Height Tertile (cm)			
140-159	89	1.02 (0.95, 1.09)	0.6346
159-170	135	1.04 (0.99, 1.09)	0.1156
170-213	113	0.99 (0.91, 1.07)	0.7831
Weight Tertile (kg)			
42-60	95	1.00 (0.94, 1.07)	0.9091
60-71	125	0.99 (0.95, 1.04)	0.7396
71-115	117	1.03 (0.98, 1.08)	0.2731
BMI Tertile (kg/m^2)			
15.59–22.90	112	0.97 (0.92, 1.03)	0.3368
22.90–25.91	111	1.03 (0.96, 1.11)	0.3558
25.91–33.32	114	1.00 (0.95, 1.05)	0.9711
TC Tertile (mmol/l)			
1.99–4.85	111	0.98 (0.92, 1.03)	0.3742
4.85–5.43	112	1.02 (0.95, 1.09)	0.5508
5.43–9.14	114	1.00 (0.96, 1.05)	0.8824
HDL-C Tertile (mmol/l)			
0.70–1.52	112	1.03 (0.98, 1.08)	0.2981
1.52–2.60	112	0.98 (0.92, 1.05)	0.6238
2.60–8.60	113	0.98 (0.94, 1.03)	0.4659
LDL-C Tertile (mmol/l)			
0.74–2.99	111	0.98 (0.93, 1.03)	0.4330
2.99–3.37	112	1.11 (1.03, 1.19)	0.0037
3.37–6.79	114	1.00 (0.95, 1.04)	0.8845
TG Tertile (mmol/l)			
0.13–1.17	112	0.99 (0.93, 1.04)	0.6276
1.17-1.45	107	1.12 (1.05, 1.20)	0.0012
1.45–6.92	118	0.94 (0.89, 0.99)	0.0215

TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; BMI, body mass index; BFP, body fat percentage; OR, odds ratio; CI, confidence interval.

Table 4
Association between potential risk factors and BCC according to baseline characteristics.

	Non-adjusted		Adjust	
	OR, 95 % CI	*P*-value	OR, 95 % CI	*P*-value
BFP (%)	1.01 (0.98, 1.04)	0.5395	1.06 (1.01, 1.11)	0.0187
BFP Tertile (%)				
Low	1.0		1.0	
Middle	0.93 (0.55, 1.58)	0.7866	1.37 (0.74, 2.53)	0.3201
High	1.22 (0.72, 2.06)	0.4578	2.64 (1.17, 5.97)	0.0196

BFP, body fat percentage; OR, odds ratio; CI, confidence interval.
Adjust model adjust for: sex (female, male); height (cm).

Ethical approval

The study was approved by the Ethics Committee of Nanjing Drum Tower Hospital and the Affiliated Hospital of Medical Collage Qingdao University, and all patients provided signed informed consent (Ethics Approval Number: 2020–365-02).

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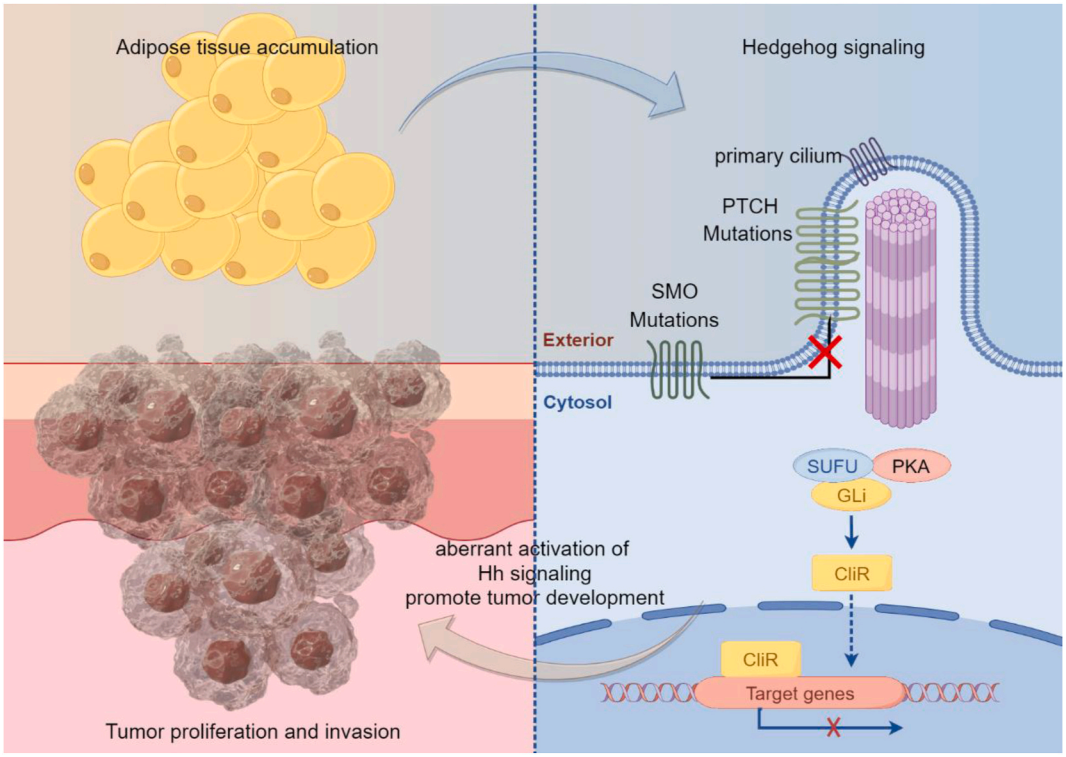

Fig. 3. Schematic representation of the proposed role of hedgehog signal in cross-talk between basal Cell Carcinoma and adipose tissue.

CRediT authorship contribution statement

Zheng Dong: Methodology, Investigation, Data curation, Conceptualization. **Zhenyu Chen:** Validation, Supervision. **Qian Tan:** Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Qian Tan reports financial support was provided by National Natural Science Foundation of China. Qian Tan reports financial support was provided by the Key Research and Development Program of Jiangsu Province, China. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35297.

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