基于单病种全程管理的鼻咽癌新型临床路径的研发与实践

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摘　要:[目的]基于单病种全程管理的理念研发鼻咽癌新型临床路径,以促进鼻咽癌的规范化诊断与治疗。[方法]以本中心鼻咽癌诊疗规范为基础设计诊疗全程的临床路径,将符合入径病例纳入路径管理,预期目标入路径率(适合入路径者/符合入路径者)≥50%;完成路径率(完成路径者/入路径者)≥70%;非预见内的变异率(非预见内的变异/入路径者)<10%。[结果]自2015年1月1日至12月31日,共收治39例新确诊鼻咽癌患者,36例符合入路径标准,100%(36/36)进入路径。完成路径率97.2%(35/36),变异率8.3%(3/36)。诊断与分期阶段、诱导化疗阶段(共3周期)、单纯放疗、同期放化疗阶段平均住院日分别为0.8、8.2、0、18.7d。单纯放疗产生的平均费用为(83 564±77)元,同期放化疗为(109 316±15 050)元,诱导化疗+同期放化疗的治疗模式产生的平均费用为(118 744±11 341)元。[结论]较高的入路径率、较高的完成路径率、较低的变异率体现了基于单病种全程管理的鼻咽癌新型临床路径有效可行,值得进一步推广应用。

关键词:临床路径;鼻咽癌;单病种管理
中图分类号:R739.63　　**文献标识码**:A　　**文章编号**:1004-0242(2017)02-0106-05
doi:10.11735/j.issn.1004-0242.2017.02.A006

A New Model of Clinical Pathway for Comprehensive Management of Nasopharyngeal Carcinoma: Research and Clinical Practice

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Abstract: [Purpose] To develop a new model of clinical pathway for comprehensive management of nasopharyngeal carcinoma(NPC), and to promote the standardization of diagnosis and treatment algorithms of NPC. [Methods] The clinical pathway was modified from the NPC protocol of the Clinical Oncology Center of the University of Hongkong—Shenzhen Hospital(HKU-SZH) and enrolled all indicated NPC patients for comprehensive management. The target enrollment ratio(patients enrolled into the pathway/patients eligible for the pathway) was more than 50%; the target completion rate (patients completed the whole pathway/patients enrolled) was more than 70%; the target rate of variation(cases of unintended variation/cases enrolled) was less than 10%. [Results] From 1st January to 31st December 2015, there were 39 cases of newly diagnosed NPC in the Clinical Oncology Center of HKU-SZH. Thirty-six of them were eligible for the clinical pathway and 100%(36/36) were enrolled. The completion rate was 97.2%(35/36) with 8.3%(3/36) of variation. Duration of hospitalization in different phases of staging workup, neoadjuvant chemotherapy (total 3 cycles), radiotherapy (RT) alone, concurrent chemo radiotherapy (CCRT) were 0.8, 8.2, 0, 18.7 days, respectively. The average cost(Yuan, RMB) for RT alone, CCRT, Neoadjuvant chemotherapy combined with CCRT were 83 564±77, 109 316 ±15 050, 118 744 ± 11 341, respectively. [Conclusions] The excellent enrollment rate, high completion rate and low variation rate illustrates feasibility of this new model of clinical pathway for comprehensive management of NPC, which deserves further nation-wide evaluation and application.

Key words: clinical pathway; nasopharyngeal carcinoma; comprehensive management of single disease

临床路径是以循证医学为指导的，用于改善医疗质量与效率的多学科诊疗工具[1]，在单病种付费中的应用属于一种新型的医疗管理方法[2,3]。现有卫生部颁发的恶性肿瘤临床路径均局限于单种治疗手段的单次住院阶段，未能反映对疾病综合治疗全程管理的关注。在鼻咽癌的诊治领域，中国卫生部门尚

收稿日期:2016-08-17;修回日期:2016-10-14
基金项目:深圳市科创委基础研究项目(JCYJ20140414092023248)
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未发布相应的临床路径。本文就香港大学深圳医院临床肿瘤中心在该领域开发的新型临床路径的前期实践,作初步探讨并报道如下。

1 资料与方法

1.1 研究对象

纳入 2015 年 1 月 1 日至 2015 年 12 月 31 日期间，香港大学深圳医院临床肿瘤中心收治新发病理诊断为鼻咽癌的患者(国际疾病分类:C11),临床分期Ⅰ、Ⅱ、Ⅲ、ⅣA、ⅣB 期(美国癌症联合委员会，AJCC 第 7 版)。排除标准:鼻咽癌ⅣC 期;病理诊断为鼻咽肉瘤、淋巴瘤等其他病理类型者。入径日期:确诊鼻咽癌后首次就诊于临床肿瘤中心时间。完成路径日期：全程治疗结束之日或全程治疗结束当次住院的出院时间。

1.2 路径制定方法

制定路径的证据引用香港大学临床肿瘤系、香港大学深圳医院临床肿瘤中心鼻咽癌治疗指引[4,5]。路径构成:分模块组合,设立各模块的完成项目与时间目标,各模块之间按照分期类别有机组合、无缝对接(Figure 1)。诊治模块分为:诊断与分期阶段、放疗前准备阶段、单纯放疗阶段、诱导化疗阶段、同期放化疗阶段、辅助化疗阶段(Table 1)。放疗采用适形调强精确放疗技术(IMRT 技术)。放化疗期间最佳支持治疗用药为临床药师监控下的为不同适应证设置的可供灵活选择的用药目录。诱导化疗、放疗疗效采用实体瘤疗效评价标准 RECIST(1.1 版),化疗、放疗副反应评价标准采用 CTCAE 3.0(Common Terminology Criteria for Adverse Events v3.0)。

1.3 统计学处理

采用 SPSS19.0 分析处理数据,计量资料采用均数±标准差或中位数表示，计数资料以频数表示。

1.4 预期目标

本临床路径对非预见的偏离路径,但不影响治疗完整度的情况定义为变异。治疗完整度至少包括如下:原计划单纯放疗者,全段放疗在合理时间段内完成；原计划同期放化疗联合诱导化疗或者辅助化疗者，至少在合理时间段内完成全段同期放化疗。否则视为退出路径。参考中国卫生部门三级医院评审标准 4.4.4.1 条款[6]:入路径率(适合入路径者/符合入路径者)≥50%；完成路径率(完成路径者/入路径者)≥70%；非预见内的变异率(非预见内的变异/入路径者)<10%。

2 结 果

自 2015 年 1 月 1 日至 2015 年 12 月 31 日,香港大学深圳医院临床肿瘤中心共收治 39 例新确诊鼻咽癌患者，其中 36 例符合鼻咽癌路径入组标准,患者中位年龄 49 岁(26~71 岁),其中男性 23 例,女性 13 例,男、女性比例为 1.77:1。Ⅰ期、Ⅱ期、Ⅲ期、ⅣA 期、ⅣB 期所占比分别为 8.3%、16.7%、41.7%、16.7%和 16.7%。

100%(36/36) 进入路径。完成路径率 97.2%(35/36),变异率 8.3%(3/36)。诊断与分期阶段、诱导化疗阶段(共 3 周期)、单纯放疗、同期放化疗阶段平均住院日分别为 0.8、8.2、0、18.7d。单纯放疗产生的平均费用为(83 564±77)元,同期放化疗为(109 316±15 050)元，诱导化疗+同期放化疗的治疗模式产生的平均费

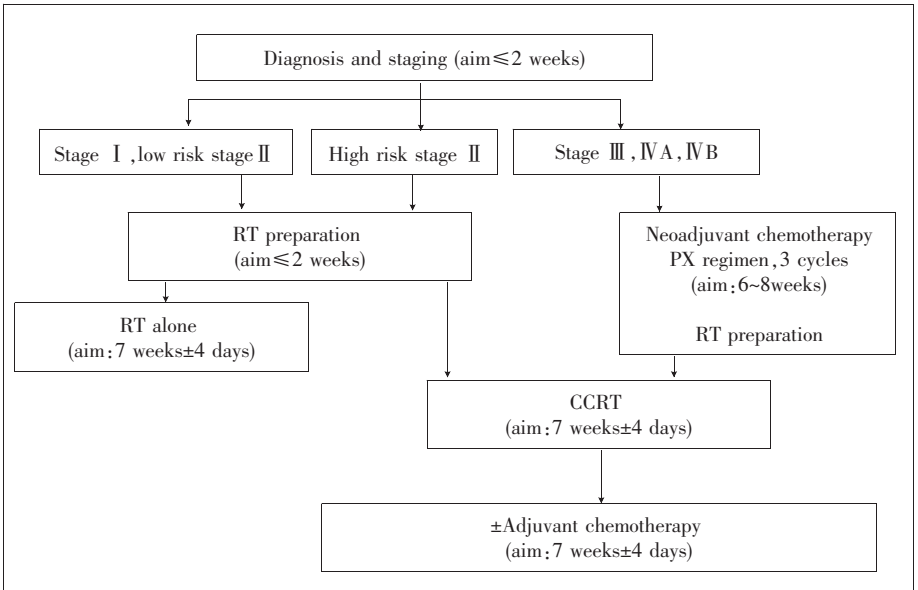

Figure 1 The HKU-SZH clinical pathway for NPC

Table 1　Detailed information of the clinical pathway

Phase	Items	Expected deviation	Corresponding management
Diagnosis and staging (aim≤2 weeks)	■ Full medical history ■ Complete blood count, liver and renal function, LDH, T4/TSH, cortisol, prolactin ■ EBV-DNA; hepatitis panel, HIV, TP ■ Nasopharyngoscopy and biopsy ■ MRI (nasopharynx + neck) ■ Bone scan * (for stage Ⅲ / Ⅳ) ■ Contrast CT Thorax & abdominal* (for stage Ⅲ / Ⅳ) ■ PET-CT (optional), if PET-CT done, omit items with * ■ Confirm staging information	■ Have been completed in other hospital ■ Service not available in this hospital	■ Do not repeat ■ Perform the items in other hospitals with available service
RT preparing (aim≤2 weeks)	■ Dental assessment (refer to odontologist) ■ CT simulation (refer to RT center) ■ Review target delineation & Treatment planning system(TPS)(clinical medical team) ■ Patient education before and during RT (oncology specialized nurses and doctors)	■ Patients need neoadjuvant chemotherapy	■ RT preparation will be done after neoadjuvant chemotherapy
RT alone Indicated for: Stage Ⅰ、low risk Stage Ⅱ (N0、GTV_P ≤ 15 cc, EBV-DNA copies≤ 4000 copies/ml) (aim: 7 weeks±4 days)	■ Confirm completion of RT preparation	None	None
CCRT Indicated for: High risk stage Ⅱ (N1、GTV_P >15 cc or EBV-DNA copies > 4000 copies/ml) (aim: 7weeks±4days)	■ Cisplatin 100mg/m^2 via intravenous infusion every 21 days for 2 cycles. The first cycle of concurrent chemotherapy is given on the first day of RT. ■ Prescription of chemotherapy strictly follow with medical administration record (MAR)	■ Creatinine clearance <60ml/min	■ Omit concurrent chemotherapy or replaced by weekly carboplatin (AUC 2)
Neoadjuvant chemotherapy Indicated for: Stage Ⅲ、ⅣA、ⅣB (aim: 6~8weeks)	■ PX regimen: cisplatin 100mg/m^2 via intravenous infusion plus capecitabine 2000 mg/m^2/day for 14 days, repeated every 21 days for 3 cycles ■ Make appointment of CT simulation on D0 of the 3rd cycle of chemotherapy ■ Make appointment of progress MRI on the D7 of the 3rd cycle of chemotherapy ■ Prescription of chemotherapy strictly follow with MAR	■ Creatinine clearance <60ml/min ■ Poor food taking	■ Replaced by carboplatin plus fluorouracil ■ Replaced by PF (Cisplatin plus fluorouracil)
Adjuvant chemotherapy Indicated for patients with suggestions by team discussion	■ PX regimen, repeated every 21 days for 3 cycles ■ Prescription of chemotherapy strictly follow with MAR	■ Creatinine clearance <60ml/min ■ Poor food taking	■ As above

用为(118 744±11 341)元(Table 2~4)。

诱导化疗后部分缓解 (partial response, PR)率为96.2%(25/26), 疾病稳定(stable disease, SD)率 3.8%(1/26)。诱导化疗期间无出现 3 度以上副反应。3 度以上放射性皮肤反应发生率为 22.2%(8/36), 3 度以上放射性口腔黏膜炎和/或放射性咽炎发生率为52.8%(19/36)。治疗结束后 8 周进行第 1 次评价, 评价项目包括鼻咽颈部 MRI、鼻咽镜、鼻咽活检。影像与病理的完全缓解率为 97.1%(34/35), 1 例行鼻咽局部推量放疗后达到完全缓解。

3　讨　论

3.1　入路径率、完成路径率

本中心鼻咽癌新型临床路径将明确适应证患者前瞻性地纳入路径管理。路径通过将各诊治阶段分

Table 2 Outcomes of clinical pathway

Indexes	Time duration (mean±SD, days)	Targeted cases	Percentage (%)
Enrollment rate	–	36/36	100.0
Completion rate	–	35/36	97.2
Variation rate	–	3/36	8.3
Diagnosis and staging	12.6±8.0	29/36	73.5
RT preparing	13.0±5.0	30/36	83.3
Neoadjuvant chemotherapy	43.4±3.5	25/26	96.2
The phase of RT alone or CCRT	51.0±5.0	32/36	88.9

Table 3 Details of unintended variations

Cases	Unintended variation	The impact to the whole treatment
No.1	CCRT after only one cycle of neoadjuvant chemotherapy	Acceptable
No.2	Refused neoadjuvant chemotherapy and received CCRT followed by 1 cycle of adjuvant chemotherapy	Acceptable
No.3	The second concurrent chemotherapy was replaced by weekly cisplatin due to grade 3 anemia	Acceptable
No.4	Diagnosed open tuberculosis infection during RT and treatment interrupted	Unacceptable, exit pathway

Table 4 The duration of inpatient stay and cost in each phase of clinical pathway (exclude PET-CT)

Phases	N	Mean inpatient day	Average cost (Yuan, RMB)
Diagnosis and staging	36	0.8	5569±3275
RT alone	3	0	83564±77
Neoadjuvant chemotherapy(total 3 cycles)	26	8.2±3.7	14950±3662
Concurrent chemotherapy(total 2 cycles)	32	4.0±0.7	3686±866
CCRT	32	18.7±13.5	116976±12419
CCRT (without neoadjuvant chemotherapy)	6	23.3±13.0	109316±15050
CCRT(with neoadjuvant chemotherapy)	26	17.7±15.5	118744±11341

解为不同模块与步骤进行有机组合从而实现诊断与分期、综合治疗的规范化,实现单病种全程管理。结果显示,本临床路径入路径率与完成路径率均达到并超过预期目标,同时优于我国卫生部统计数据报告的路径完成率(89.43%)[7],以及国内某肿瘤专科医院报道的入路径率(45.15%)和路径完成率(25.63%)[8]。新型临床路径从整体架构上为鼻咽癌单病种各分期诊断设置了清晰、灵活、实用的全程诊疗地图,便于临床路径的开展与实施,从而提高入路径率和完成路径率。

3.2 各模块所需的时间目标

本路径为每个诊疗模块设置了时间目标,不限于门诊或住院的形式完成,非拘泥于严格控制单次住院期间各诊疗项目的执行时间标准,从而提高了临床医生实施路径的灵活度。在此路径下,100%的患者可以完成必须诊疗的项目。诊断与分期阶段仅73.5%达到时间目标、确定分期后放疗计划设计阶段时间达标率仅 83.3%,主要与医疗资源的不足导致预约周期延长、尚无信息管理系统实现自动化提醒等因素有关。为临床路径患者设置优先权重以及信息化管理有助于改进时间目标的控制。诱导化疗阶段的时间达标率为 100%,可能与化疗的耐受性较好、依从性较好有关。同期放化疗阶段88.9%的患者在既定时间目标内完成,分析导致放疗延期的因素包括放疗期间出现的导致放疗中断的并发症、5d以上的法定假日等。

3.3 变异率分析

国内外关于变异的管理和评价有不同的理念和方法[9]。本新型临床路径对非预见的偏离路径,但不影响治疗完整度的情况定义为变异。路径预见性地考虑了治疗过程中可能存在的变异,如可能存在肌酐清除率差异导致化疗药物的选择变异等,从而进行相应的合理调整,保障入路径患者可以最大限度完成路径。除此外的偏离路径却未影响既定治疗完整度目标则定义为变异。本组数据显示变异率为 8.3%,低于文献报道的 17.8%[8]。科学合理的变异设置有助于路径在日常诊疗工作中的推广。

3.4 平均住院日分析

本研究中,3 周期诱导化疗阶段的总体平均住院日为 8.2d,2 周期同期化疗平均住院日为 4d;放疗期间的总体平均住院日约 0~23d,显著低于国内报道的数据[10]。这主要与本路径的实施过程不限于门诊与住院的形式有关。中国卫生部现发行的肿瘤临床路径多基于单病种的某一项治疗手段的单次住院分析,基于单次住院医嘱与时间的严格限制,不利于灵活安排诊疗项目的实现形式,反而不利于达到降低住院日、节约医疗资源的目标,同时也不能体现恶

性肿瘤全程综合治疗的多学科团队合作以及对单病种持续、整体的管理。

3.5 费用分析

化疗与最佳支持治疗是疾病治疗中可能产生费用差异最大的两个环节。本临床路径对每个化疗方案制定了专用处方模板(即 MAR),包含化疗药物以及防治化疗副反应的药物配置,每位患者仅需计算并填写精确化疗药物剂量,即可生成整个化疗周期的医嘱,从而保障了路径的规范性实施。放化疗期间最佳支持治疗用药为临床药师监控下的为不同适应证设置的可供灵活选择的用药目录,保障临床一线医生开立医嘱的标准化与个体化。此样本平均诊疗费用与某省肿瘤医院 2015 年度鼻咽癌住院治疗总费用预测值 106 299 元[11]较为相当,因尚缺乏相同治疗模式下其他医院的治疗费用报道,因此暂无法与非路径或者其他医院费用进行对比。

3.6 小 结

本临床路径以鼻咽癌单病种管理为出发点,为不同诊疗阶段设置独立、有机结合、灵活操作的模块,进而为每个模块设置相应的规范化步骤,其较高的入路径率与完成路径率、较低的变异率体现了本临床路径有效可行,值得进一步推广应用。未来将与信息技术部门合作,实现本临床路径的电子化监控。长期控制率与生存率将持续跟进随访分析。

参考文献:

[1] Vanhaecht K,Bollmann M,Bower K,et al. Prevalence and use of clinical pathways in 23 countries——an international survey by the European Pathway Association [J]. Journal of Integrated Care Pathways,2006,10 (1):28–34.

[2] Kreys ED,Koeller JM. Documenting the benefits and cost savings of a large multistate cancer pathway program from a payer's perspective [J]. J Oncol Pract,2013,9(5):e241–e247.

[3] Song FF,Zhao KY,Shen JL. Application research progress of clinical pathway in single disease[J]. China Medical Herald,2016,13(3):163–165. [宋斐斐,赵坤元,申俊龙. 临床路径在单病种付费中的应用研究进展[J]. 中国医药导报,2016,13(3):163–165.]

[4] Lee AW,Ma BB,Ng WT,et al. Management of nasopharyngeal carcinoma:current practice and future perspective [J]. J Clin Oncol,2015,33(29):3356–3364.

[5] Lee AW,Ngan RK,Tung SY,et al. Preliminary results of trial NPC-0501 evaluating the therapeutic gain by changing from concurrent-adjuvant to induction-concurrent chemoradiotherapy,changing from fluorouracil to capecitabine,and changing from conventional to accelerated radiotherapy fractionation in patients with locoregionally advanced nasopharyngeal carcinoma[J]. Cancer,2015,121(8):1328–1338.

[6] National Health and Family Planning Commission of the People's Republic of China. Details of implementation for evaluation of class 3A hospital(2011 version)[DB/OL]. http://www.nhfpc.gov.cn,2016–07–15.[中华人民共和国国家卫生和计划生育委员会. 三级综合医院评审标准实施细则 (2011 年版)[DB/OL].http://www.nhfpc.gov.cn,2016–07–15.]

[7] Zhao K,Zhang Y,Ma L,et al. Evaluation of the effectiveness and current status of clinical pathway management trials in public hospitals:based on data collected through the clinical pathway platform[J]. Chinese Health Economics,2013,32(359):76–80. [赵琨,张莹,马莉,等. 公立医院临床路径管理试点工作开展现状与效果评估: 基于卫生部临床路径上报数据[J]. 中国卫生经济,2013,32(359):76–80.]

[8] Liu G,Xiang MF,Zou J,et al. Application analysis of the clinical pathway in a tumor hospital[J]. Sichuan Medical Journal,2015,36(8):1095–1098.[刘罡,向明飞,邹江,等. 临床路径在肿瘤专科医院应用情况分析[J]. 四川医学,2015,36(8):1095–1098.]

[9] Liu PZ,Tao HB,Wu GH,et al. Status quo analysis of variations management of clinical pathways in China and abroad[J]. Chines Journal of Hospital Administration,2011,27(2):100–103. [刘鹏珍,陶红兵,武广华,等. 国内外临床路径变异管理的现状分析[J]. 中华医院管理杂志,2011,27(2):100–103.]

[10] Zhang YH,Kan JY,Chen B,et al. The effect of clinical pathway in the locally advanced nasopharyngeal carcinoma [J]. Guangdong Medical Journal,2012,33(24):3779–3780. [蟑耀鸿,刊健泳,陈冰,等. 临床路径在局部中晚期鼻咽癌中的实施效果[J]. 广东医学,2012,33(24):3779–3780.]

[11] Liao XZ,Shi BG,Xu KK,et al. An analysis of hospitalization expenses of 9 kinds of malignancy in a provincial cancer hospital,2004~2010[J]. China Cancer,2012,21(12):917–921. [廖先珍,史百高,许可葵,等. 2004~2010 年某省级肿瘤专科医院 9 种恶性肿瘤住院费用分析[J]. 中国肿瘤,2012,21(12):917–921.]