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Tabel dan Gambar

Tabel harus singkat dan jelas. Judul table hendaknya ditulis di atasnya dan catatan di bawahnya. Jelaskan semua singkatan yang dipergunakan. Gambar hendaknya jelas dan lebih disukai bila telah siap untuk dicetak. Judul gambar ditulis di bawahnya.

Asal rujukan table atau gambar dituliskan di bawahnya. Tabel dan gambar hendaknya dibuat dengan program Power Point, Free Hand, atau Photoshop, (menggunakan format jpeg).

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Jurnal

1. *Naskah dalam majalah/jurnal*
   Gracey M. The contaminated small-bowel syndrome: pathogenesis, diagnosis, and treatment. Am J Clin Nutr 1979; 32:234-43.
2. *Organisasi sebagai pengarang utama*
   Direktorat Jenderal PPm & PLP, Departemen Kesehatan Republik Indonesia. Pedoman pengobatan malaria. Medika 1993; 34-23-8.
3. *Tanpa nama pengarang*
   Imaging of sinusitis [editorial]. Ped Infect J 1999; 18:1019-20.
4. *Suplemen*
   Solomkim JS, Hemsel DL, Sweet R, dkk. Evaluation of new infective drugs for the treatment of intrabdominal infections. Clin Infect Dis 1992, 15 Suppl 1:S33-42.

Buku dan Monograf

1. *Penulis pribadi*
   Banister BA, Begg NT, Gillespie SH. Infectious Disease. Edisi pertama. Oxford: Blackwell Science; 1996.
2. *Penulis sebagai penyunting*
   Galvani DW, Cawley JC, Penyunting. Cytokine therapy. New York: Press Syndicate of University of Cambridge; 1992.
3. *Organisasi sebagai penulis dan penerbit*
   World Bank. World development report 1993; investing in health. New York: World Bank; 1993.
4. *Bab dalam buku*
   Loveday C. Virogoly of AIDS. Dalam: Mindel A, Miller R, penyunting. AIDS, a pocket book of diagnosis and management. Edisi kedua. London: Arnold Holder Headline Group; 1996. H. 19-41.
5. *Attention: konferensi*
   Kimura j, Shibasaki H, penyunting. Recent advanced in clinical neurophysiology. Presiding dari the 10th International 15-19 Oktober 1995.
6. *Naskah konferensi*
   Begston S, Solheim BG, Enforcement of data protection, privacy and security in medical informatics. Dalam : Lun KC, Degoultet P, Piemme TE, Reinhoff o, penyunting MEDINFO 92. Presiding the 7th World Congress on Medical Informatics: Sep 6-10, 1992; Genewa, Swiss. Amsterdam: North Holland; 1993. H. 1561-5.
7. *Laporan ilmiah*
   Akutsu T. Total heart replacement device. Bethesda: National Institute of Health, Nation Heart and Lung Institute; 1974 Apr. Report No: NHH-NHL1-69-2185-4.
8. *Disertasi*
   Suyitno RH. Pengamatan vaksinasi dalam hubungannya dengan berbagai tingkat gizi [disertasi]. Semarang: Fakultas Kedokteran Universitas Diponegoro, 1983.

Publikasi lain

1. *Naskah dalam Koran*
   Bellamy C. Gizi bayi adalah investasi masa depan. Kompas 26 Januari 2000; hal 8 kolom 7-8.
2. *Naskah dari audiovisual*
   AIDS epidemic: the physician's role [rekaman video]. Cleveland: Academy of Medicine of Cleveland, 1987.
3. *Naskah belum dipublikasi (sedang dicetak)*
   Connellv KK. Febrile neutrDpenia. J Infect Dis. In press.
4. *Naskah Jurnal dalam bentuk elektronik*
   Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] Jan-Mar 1995 [cited 5 Jan 1996] 1910: [24 screen]. Didapat dari URL: http\\www.cdc.gov/ncidod/EID/eid.htm.
5. *Monograf dalam format elektronik*
   CDI. LliniGiil dermatology illustrated [monograph pada enROM]. Reeves JRT, Maibach H, CMEAMultimedia Lnnip, produser, edisi ke-2. Versi 2.0. San Diego: CMEA; 1995.
6. *Naskah dari file computer*
   Hemodynamics III: the ups and down of hemodynamics [program computer]. Versi 2.2. Orlando (F-L); Computerized Educational System; 1993.

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Daftar Isi

Tren Tata Laksana Kanker Prostat Lokal Lanjut di Indonesia

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ABSTRACT

Aim: to evaluate treatment trend of stage T3 prostate cancer based on several factors. Methods: a retrospective study was done on stage T3 prostate cancer patients from year 1995-2013, at two national referral hospitalsin Indonesia. Treatment trends between hormonal therapy and radiotherapy based on year of treatment, PSA level, tumor grade and age groups were evaluated.Results: On 50 patients subjects, 25 (50%), 23 (46%) and 2 (4%) subjects were treated by radiotherapy, hormonal therapy and radical prostatectomy, respectively. Year of treatment were significantly associated with treatment selection (p=0.012), after excluding year of treatment 1995-1999 group. Hormonal therapy was preferred on high grade tumor group (53.8%) and more applied for older patients. Treatment trend was not affected by PSA level. Conclusion: Year of treatment were significantly associated with treatment selection of stage T3 prostate cancer. Hormonal therapy was preferred on high grade tumor group and older age groups.

Keyword: *treatment trend, locally advanced prostate cancer, radiotherapy, hormonal therapy*

ABSTRAK

Penelitian ini bertujuan mengevaluasi tren tata laksana kanker prostat *stage* T3 berdasarkan faktor-faktor yang memengaruhi. Metode: studi retrospektif tata laksana kanker prostat *stage* T3 di Rumah Sakit Cipto Mangunkusumo dan Rumah Sakit Kanker "Dharmais" periode 1995-2013. Data tren pemilihan terapi antara radioterapi atau terapi hormonal dianalisis berdasarkan kelompok tahun terapi, kadar PSA, *grade* tumor, dan kelompok usia. Hasil penelitian menunjukkan dari 50 subjek, 25 (50%), 23 (46%), dan 2 (4%) subjek mendapatkan tata laksana radioterapi, terapi hormonal, dan prostatektomi radikal secara berturutan. Perubahan tren pemilihan terapi berdasarkan tahun terapi secara statistik signifikan (p=0,012), dengan mengeksklusikan kelompok periode terapi 1995-1999. Terapi hormonal lebih menjadi pilihan untuk kelompok tumor *high grade* (53,8%) dan lebih sering dipilih seiring bertambahnya usia pasien. Kadar PSA tidak memengaruhi tren pemilihan terapi. Kesimpulan: terdapat perubahan yang bermakna dalam pemilihan terapi kanker prostat *stage* T3 berdasarkan tahun terapi. Terapi hormonal lebih menjadi pilihan pada kasus dengan tumor *high grade* dan kelompok usia yang semakin tua.

Kata Kunci: tren terapi, kanker prostat lokal lanjut, radioterapi, terapi hormonal

Efek Laserpunktur pada Titik MA-TF1 Shenmen dan MA-AT Kelenjar Parotis terhadap Gejala Xerostomia Pasien Kanker Nasofaring Pasca-radioterapi

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ABSTRACT

Xerostomia (dry mouth) is a chronic and acute effect on a cancer patient who receives radiation therapy on the areas of head and neck. Earlier studies state that acupuncture helps to relieve the symptoms concerning cancer and xerostomia is one. Laserpuncture is an acupuncture therapy technique that uses the benefit of low energy laser beam that does not generate pain and is not an invasive procedure which is more comfortable for patients. This research involved 44 xerostomia patients who have underwent complete radiotherapy on the minimum course of 3 months up to a maximum of 1.5 years before going through with the research; the research is clustered into ear laserpuncture and sham laserpuncture groups. The result shows a mean Xerostomia Inventory (XI) score between two states of pre against post laserpuncture of 3 and 6 times of treatment that were tested on case group and control group; there is a mean score of life quality of pre treatment compared to post treatment of laserpucture on those who underwent 3 times and 6 times laserpucture treatment on case group and control group on every variable of life quality, except financial difficulties (FI); and there is a mean pH score on the saliva of those undergoing treatment between the states of pre and post 6 times laserpuncture treatment on case group and control group. From this study, we can conclude that laserpuncture on ear acupoints MA-TF1 Shenmen and MA-AT parotis gland might increase saliva pH and reduce XI score, and we can considered as an adjuvant treatment in xerostomia on cancer patients post radiotherapy.

Keyword: *ear laserpuncture; xerostomia Inventory; pH saliva; life quality.*

ABSTRAK

Xerostomia (mulut kering) merupakan efek akut dan kronik pada pasien kanker yang mendapat terapi radiasi pada daerah kepala dan leher. Beberapa studi pendahuluan mengemukakan bahwa akupunktur meringankan gejala atau keluhan yang berhubungan dengan kanker, di antaranya xerostomia. Laserpunktur merupakan teknik terapi akupunktur yang memanfaatkan sinar laser energi rendah yang tidak menimbulkan rasa nyeri serta tidak invasif

sehingga lebih nyaman bagi pasien. Penelitian ini melibatkan 44 pasien xerostomia yang telah menjalani radioterapi lengkap minimal 3 bulan dan maksimal 1,5 tahun sebelum mengikuti penelitian. Pasien dibagi menjadi kelompok laserpunktur telinga dan kelompok laserpunktur *sham*. Hasil penelitian menunjukkan terdapat rerata selisih skor *Xerostomia Inventory* (XI) antara sebelum tindakan laserpunktur dengan setelah memperoleh tindakan laserpunktur 3 kali dan 6 kali pada kelompok kasus dan kontrol. Terdapat rerata selisih skor kualitas hidup antara sebelum tindakan laserpunktur dengan setelah memperoleh tindakan laserpunktur 3 kali dan 6 kali pada kelompok kasus dan kontrol pada semua variabel kualitas hidup, kecuali variabel *financial difficulties* (FI). Terdapat rerata selisih pH saliva antara sebelum tindakan laserpunktur dengan setelah memperoleh tindakan laserpunktur 6 kali pada kelompok kasus dan kontrol.

Dari hasil penelitian ini dapat disimpulkan bahwa laserpunktur pada titik akupunktur telinga MA-TF1 Shenmen dan MA-AT kelenjar parotis dapat meningkatkan pH saliva dan menurunkan skor XI sehingga dapat dipertimbangkan sebagai salah satu penunjang pengobatan xerostomia pada pasien kanker nasofaring pasca-radioterapi.

Kata Kunci: laserpunktur telinga; *xerostomia Inventory*; pH saliva; kualitas hidup.

Hubungan antara *Genotyping* DNA *Human Pappillomavirus* (HPV) dengan Respons Terapi Radiasi pada Adenokarsinoma Serviks

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ABSTRACT

The object of this study to know the type of DNA Human Papilloma Virus genotyping in adenocarcinoma cervical cancer, espescially in Cipto Mangunkusomo Hospital and Cancer Centre Dharmais Hospital. The importance of human papilloma virus (HPV) infection in the outcome of cervical cancer afterradiotherapy remains unknown. Our study explored whether the HPV status of tumors and also persistence of the HPV infection is related with the outcome of radiotherapy in patients with cervical cancer.

The biopsy cervix samples taken from 12 patients with Adenocarcinoma cervical cancer (Stage IIB-IIIB) that met in the inclusion criteria. The HPV genotyping examination was conducted twice, before and 3 month after radiation therapy. The subjects treated by radiation therapy without sensitizer according to standard procedures. After underwent complete radiation, responsse of radiation therapy was conducted by clinical assessment and repeated HPV genotyping test.

Result: a total of 12 patients had been collected in this study. From this sample, there were found HPV-positive tumors in 91,7% (11 cases) of patients, with the details of a single infection of 75% and 16,7% multiple infections. Based on the type of HPV type 18 was obtained (66,7%), type 45: 8,3%. Persistent infection with HPV after radiation encountered by 41,7%. Complete clinical responsse observed in the single infection group number of 66,7%, while in the group of multiple infections by 50% (p = 1,000). While HPV infection settled with a complete clinical responsse by 16,7% (p = 0,015).

There weren't clinically relationships between clinical complete responsse with single or multiple HPV infection (p = 1,000). There were clinically relationship between persistent HPV infection with complete clinical responsse (p = 0,015).

Keyword: *cervical cancer, genotyping HPV DNA, persistent infection, clinical response*

ABSTRAK

Penelitian ini bertujuan untuk mengetahui jenis genotipe DNA HPV pada kasus adenokarsinoma serviks , terutama di RSUPN Cipto Mangunkusumo dan RS Kanker "Dharmais". Penelitian ini juga bertujuan untuk mengetahui hubungan antara genotipe DNA HPV dengan respons klinis radiasi serta mengetahui terjadinya infeksi HPV menetap respons klinis terapi radiasi.

Dua belas penderita kanker serviks stadium IIB-IIIB dengan hasil histopatologi adenokarsinoma serviks sesuai dengan kriteria inklusi dilakukan pemeriksaan genotipe HPV DNA yang berasal dari biopsi serviks. Sampel penelitian diberikan tata laksana dengan terapi radiasi tanpa sensitizer sesuai prosedur standar. Tiga bulan setelah dinyatakan selesai radiasi, dilakukan penilaian respons klinis radiasi dan pemeriksaan genotipe DNA HPV ulang.

Dari 12 sampel penelitian, didapatkan infeksi HPV sebelum radiasi 11 sampel (91,7%) dengan perincian infeksi tunggal 75% dan infeksi multipel 16,7%. Berdasarkan tipe HPV, diperoleh infeksi tunggal tipe 18 (66,7%) dan tipe 45 (8,3%). Infeksi menetap HPV setelah radiasi, baik pada infeksi tunggal maupun multipel sebesar 41,7%. Respons klinis komplit dijumpai pada kelompok infeksi tunggal sejumlah 66,7%; sedangkan pada kelompok infeksi multipel sebesar 50% (p=1,000) dan infeksi HPV menetap dengan respons klinis komplit sebesar 20,0% (p=0,015).

Penelitian ini menyimpulkan bahwa tipe HPV DNA terbanyak dijumpai pada penderita adenokarsinoma serviks adalah tipe 18, yaitu 83,4%. Infeksi HPV menetap setelah radiasi sebanyak 41,7%. Tidak terdapat perbedaan respons klinis antara infeksi tunggal dan infeksi multipel HPV, tetapi tidak terdapat hubungan yang signifikan (p=1,000). Infeksi menetap HPV berhubungan secara klinis dengan respons klinis terapi radiasi (p=0,015).

Kata Kunci: kanker serviks, adenokarsinoma, tipe DNA HPV, infeksi HPV menetap, respons terapi.

Sacral Tumor: Experience in a Single Institution

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ABSTRACT

Introduction. *Sacral tumors are rare, and experience of these tumors is usually limited to a small number of patients. In this study, we evaluated profile, survival rates, and functional outcome in a series of sacral tumor treated in our institution.*

Method. *We retrospectively reviewed the records of 22 sacral tumor patients from January 1995 to February 2014 in Cipto Mangunkusumo National Central Hospital, Jakarta, Indonesia. Kaplan-Meier method was used to described survival and functional outcome. Their correlation with clinical profile, histological type, level of sacral involvement, treatment, and complication were analyzed by Log rank test.*

Results. *From 22 patients, 5 of them were excluded from this study. Thus, there were 17 cases of sacral tumor, 16 of them were malignant and one case was benign. In Kaplan-Meier Analysis, there were no significant difference in survival found between sex, age group, biopsy type, level of sacral involvement, treatment, and complication. There was significant difference in survival found between histopathology result (p=0.012), and giant cell tumor GCT showed the highest survival, followed by chordoma, metastatic lession, and Ewing Sarcoma. Sacral tumor at the level of S2 and below had better functional outcome compared to the one above S2 (p=0.001). There were no difference in functional outcome found between histopathology type and treatment (p=0.137 and p=0.210).*

Conclusion. *The majority of primary tumors of sacrum are chordoma which present with nonspecific early signs and symptoms. Survival rate and functional outcome of the sacral tumor patients were determined by histopathology result and level of sacral involvement. Lower level of sacral involvement lead to better survival and functional outcome.*

Keyword: *sacral tumors, chordoma, giant-cell tumor, metastasis, survival, functional outcome*

ABSTRAK

Pendahuluan. Tumor sakrum sangat jarang ditemukan; dan pengalaman mengenai tumor sakrum biasanya terbatas pada sejumlah kecil pasien. Dalam studi ini, kami mengevaluasi profil, tingkat kesintasan, dan luaran fungsional dari serangkaian tumor sakrum yang dirawat di institusi kami.

Metode. Kami telah mengevaluasi 22 pasien tumor sakrum dari Januari 1995 sampai Februari 2014 secara retrospektif di Rumah Sakit Umum Pusat Nasional Cipto Mangunkusumo Jakarta Indonesia. Metode Kaplan-Meier digunakan untuk menganalisis angka kesintasan dan luaran fungsional. Hubungan antara kesintasan dan luaran fungsional dengan profil klinis, jenis histopatologi, level sakrum yang terlibat, penatalaksanaan, dan komplikasi dianalisis dengan Log rank test.

Hasil. Dari 22 pasien, hanya 17 pasien tumor sakrum yang dimasukkan ke dalam studi ini (5 kasus diekslusi), 16 kasus dengan tumor ganas dan 1 kasus dengan tumor jinak. Hasil analisis Kaplan-Meier menunjukkan tidak ada perbedaan yang bermakna pada angka kesintasan terhadap jenis kelamin, kelompok umur, jenis biopsi, level sakrum yang terlibat, penatalaksanaan, dan komplikasi. Hasil uji statististik menunjukkan perbedaan yang bermakna antara kesintasan dengan hasil histopatologi (p = 0,012), giant cell tumor menunjukkan kesintasan hidup tertinggi, diikuti oleh Chordoma, lesi metastasis, dan Ewing Sarcoma. Tumor sakrum setinggi S2 ke bawah memiliki luaran fungsional yang lebih baik dibandingkan dengan level di atas S2 (p = 0,001). Hasil uji statistik menunjukkan tidak ada perbedaan yang bermakna antara luaran fungsional dengan jenis histopatologi dan penatalaksanaan (p = 0,137 dan p = 0,210).

Kesimpulan. Mayoritas tumor primer pada tulang sakrum adalah chordoma yang muncul dengan gejala dan tanda-tanda awal yang tidak spesifik. Angka kesintasan dan luaran funsional pasien tumor sakrum dipengaruhi oleh jenis histopatologi dan level sacrum yang terlibat. Semakin rendah level sacrum yang terlibat, semakin baik kesintasan dan luaran fungsional.

Kata Kunci: Tumor sakrum, Chordoma, giant cell tumor, metastasis, kesintasan, luaran fungsional

Hubungan Ekspresi Protein Bcl-2 Jaringan dengan *Disease Free Survival* 2 Tahun Pasien Kanker Epitel Ovarium di Rumah Sakit Dr. Soetomo, Surabaya

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ABSTRACT

Ovarian cancer is one of the most common causes of death among gynecological malignancies. Previous reports have shown that the anti-apoptotic protein Bcl-2 is over expressed in many solid neoplasms, including ovarian cancers, and contributes to neoplastic transformation and drug-resistant disease, resulting in poor clinical outcome.

This study is an observational descriptive cross-cut design to determine the role of Bcl-2 protein expression as a two year disease free survival prognostic factor in patients with epithelial ovarian cancer. Data were extracted from 37 patients treated with primary surgery with or with out secondary surgery followed by adjuvant therapy, from January 1st2010 to December 31st2011, at the Division of Gynecologic Oncology, Department of Obstetric and Gynecology, Medical Faculty of Airlangga University, Surabaya, Indonesia, were retrospectively analyzed. Bcl-2 expression were analized by immunohistochemistry study. The reccurency evaluation was done by CT-scan. The time to follow-up was 24 months since patients diagnosis. Spearman and Phi correlation test were used for analysis. In this study, two year disease free survival rate of patients was found 78.4% (29 of 37), respectively, and Spearman and Phi correlation test showed that there were no significant relation between Bcl-2 expression and ovarian cancer recurrence (p=0.084).

Expression of Bcl-2 as an anti-apoptotic protein in ovarian cancer was not significantly related with the tumor reccurency as a marker of the two year disease free survival.

Keyword: *ovarian cancer, Bcl-2 protein expression, two year disease free survival*

ABSTRAK

Kanker ovarium merupakan salah satu penyebab terbanyak kematian karena kanker ginekologi. Penelitan sebelumnya menunjukkan bahwa protein anti-apoptosis Bcl-2 ter-*over-expressed* pada banyak neoplasma solid, termasuk kanker ovarium; juga berkontribusi pada transformasi neoplasma dan resistansi terhadap kemoterapi yang menyebabkan luaran klinis kurang baik.

penelitian Ini adalah observasional deskriptif dengan rancangan potong silang untuk melihat peran ekspresi protein Bcl-2 sebagai faktor prognostik *disease free survival* 2 tahun pada pasien kanker epitel ovarium. Data diambil dari 37 pasien yang menjalani operasi primer dengan/tanpa operasi sekunder yang diikuti dengan kemoterapi ajuvan, dari 1 Januari 2010 sampai dengan 31 Desember 2011, di Divisi Onkologi Ginekologi, Departemen Obstetri dan Ginekologi, Fakultas Kedokteran Universitas Airlangga, Surabaya, Indonesia, dianalisis secara retrospektif. Ekspresi Bcl-2 diperiksa dengan teknik histokimia. Evaliasi rekurensi dilakukan dengan pemeriksaan CT-scan. Pemeriksaan dilakukan pada pasien yang sudah 2 tahun terdiagnosis kanker ovarium. Uji korelasi Spearman dan Phi dipergunakan untuk analisis data.

Hasil penelitian menunjukkan angka bebas tumor 2 tahun sebesar 78,4% (29 dari 37), dan uji korelasi Spearman serta Phi menunjukkan bahwa tidak ada hubungan yang bermakna antara Bcl-2 dengan angka bebas tumor yang ditunjukkan dengan rekurensi tumor (p=0,084).

Kesimpulannya, ekspresi protein sebagai protein anti-apoptosis pada kanker ovarium tidak berhubungan secara bermakna dengan rekurensi tumor sebagai petanda angka bebas tumor 2 tahun.

Kata Kunci: kanker ovarium, ekspresi protein Bcl-2, angka bebas tumor 2 tahun.

Kolangiokarsinoma dan Infeksi Virus Hepatitis

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ABSTRACT

Cholangiocarcinoma is a cancer which derived from biliary epithelial. This malignancy is rare, but have poor prognosis. Manifestation of liver flukes, primary sklerosing cholangitis, hepatolithiasis, and malformation of the biliary tree all this time are known to be risk factors for cholangiocarcinoma. In recent years, it has been shown that infection of hepatitis B and hepatitis C viral are also cholangiocarcinogenic, so it is known to become 'new' risk factor for cholangiocarcinoma. A literature study was conducted to search for pathogenesis theory and evidence in clinical and community study. Most basic, epigenetic, pathologic, clinical, and community studies revealed that there is a link between hepatitis viral infection and intrahepatic cholangiocarcinoma. Unfortunately, the link between the infection and extrahepatic cholangiocarcinoma remain unclear. Look at the analysis, in the future, we must take more attention to

chronic hepatitis patients for the risk of getting cholangiocarcinoma, while in cholangiocarcinoma, we must also consider about the risk factors such as hepatitis viral infection in the patients.

Keywords: *cholangiocarcinoma, hepatitis B, hepatitis C, cholangiocarcinogenic*

ABSTRAK

Kolangiokarsinoma adalah kanker yang berasal dari epitel bilier. Keganasan ini termasuk jarang, namun memiliki prognosis yang buruk. Manifestasi cacing hati, kolangitis sklerosis primer, hepatolitiasis, dan malformasi bilier selama ini diketahui merupakan faktor risiko kejadian kolangiokarsinoma. Beberapa tahun terakhir diketahui bahwa infeksi virus hepatitis B dan hepatitis C juga memiliki sifat kolangiokarsinogenik sehingga menjadi faktor risiko 'baru' bagi kejadian kolangiokarsinoma. Penelusuran literatur mengenai patogenesis dan bukti ilmiah dalam studi klinis dan epidemiologi dilakukan untuk mengkaji hubungan antara infeksi virus hepatitis B dan C dengan kolangiokarsinoma. Sebagian besar riset dasar, epigenetik, patologi, klinis, dan komunitas (populasi) menyiratkan adanya hubungan antara infeksi virus hepatitis B dan C dengan kolangiokarsinoma intrahepatik. Sayangnya, hubungan infeksi kedua virus dengan kolangiokarsinoma ekstrahepatik masih belum jelas. Melihat kajian ini, ke depan perlu perhatian lebih kepada pasien hepatitis kronis terhadap risiko kolangiokarsinoma. Sementara, bagi pasien kolangiokarsinoma, perlu pencarian faktor risiko, yang salah satunya adalah infeksi virus hepatitis kronis.

Kata Kunci: kolangiokarsinoma, hepatitis B, hepatitis C, kolangiokarsinogenik

pada 90 hari pertama dari awal mulainya radioterapi atau 4 sampai 6 minggu setelah radioterapi berakhir. Setelah itu, efek akut dianggap telah pulih dan mulailah muncul efek lanjut. Efek lanjut ini bisa jadi adalah komplikasi dari efek akut.[20]

Berdasarkan definisi efek akut dan kronik tersebut maka untuk mencegah kerancuan dengan efek akut, penelitian ini memasukkan kriteria subjek harus telah melalui waktu pemulihan 3 bulan setelah tanggal radiasi terakhir sehingga hanya efek lanjut yang diamati.

Pada penelitian ini ditetapkan dosis radioterapi ~ 70 Gy mengingat dosis yang diberikan pada terapi KNF adalah 180–200 cGy per fraksi, 5 kali dalam seminggu, sehingga dosis mencapai 66-70 Gy dengan memperhatikan lapangan radiasi.[2,21] Selain itu, kerusakan kelenjar saliva masih dapat kembali membaik bila disebabkan oleh radiasi dengan dosis <50 Gy. Kerusakan tersebut bersifat permanen bila terpapar oleh radiasi dengan dosis tinggi.[22]

Pada penelitian ini, terapi laserpunktur dilakukan 6 kali, berdasarkan penelitian sebelumnya yang dilakukan oleh Garcia MK, dkk. (2009).[23] Pada penelitian Garcia MK, dkk. (2009) didapatkan hasil bahwa terjadi penurunan skor XI setelah dilakukan terapi akupunktur selama 3 minggu atau 6 kali.[23] Hasil penelitian ini sesuai dengan penelitian Garcia MK, dkk. (2009) di mana setelah terapi laserpunktur 6 kali terjadi penurunan skor XI. [23]

Laserpunktur merupakan teknik terapi akupunktur yang memanfaatkan sinar laser energi rendah yang menggantikan jarum akupunktur. Teknik ini memiliki beberapa keunggulan dibandingkan teknik akupunktur dengan jarum, antara lain tidak menimbulkan rasa nyeri dan tidak invasif sehingga lebih nyaman bagi pasien.[13] Selain itu, laserpunktur tidak menimbulkan efek samping berkeringat banyak, pusing, rinitis, mual, sering buang air kecil, takikardi, dan gangguan visus seperti yang sering ditimbulkan oleh obat-obatan.

Bila dibandingkan dengan obat-obatan pengganti atau stimulan saliva lain, termasuk pilocarpine, terapi laserpunktur telinga mampu memberikan hasil yang baik dengan efek samping minimal. Dengan demikian, terapi laserpunktur telinga dapat berperan sebagai terapi suportif pada pasien KNF pasca-radioterapi 3 bulan hingga 1,5 tahun yang mengalami xerostomia. Laserpunktur juga efektif mengurangi keluhan pasien sehingga pasien mampu meningkatkan kualitas hidupnya.

KESIMPULAN

Hasil penelitian ini menyimpulkan bahwa laserpunktur pada titik akupunktur telinga MA-TF1 Shenmen dan MA-AT kelenjar parotis dapat meningkatkan pH saliva dan menurunkan skor XI sehingga dapat dipertimbangkan sebagai salah satu penunjang pengobatan xerostomia pada pasien kanker nasofaring pasca-radioterapi.

DAFTAR PUSTAKA

1. Roezin A. Kanker Nasofaring. Kursus Singkat Pencegahan, Deteksi Dini dan Pengobatan Kanker, Jakarta, FKUI/RSCM, 1994, hal 102-9.
2. Gondhowiardjo S, dkk. Pedoman Tata Laksana Kanker. Ed.1. Jakarta, Badan Penerbit FKUI, 2010, 27-38.
3. Departemen Radioterapi RSUPN Dr. Cipto Mangunkusumo Jakarta 2011.
4. Kuthasema P. Experience of xerostomia management and outcome in patients with head and neck cancer post radiation. Descriptive research. Thesis. Bangkok: Faculty of Graduate Studies Mahidol University 2008.
5. Dirix P, Nuyts S, Bogaert WV. Radiation-induced xerostomia in patients with head and neck cancer. *Cancer* 2006; 107:2525-34.
6. Dreizen S, Brown LR, Handler S, Levy BM. Radiationinduced xerostomia in cancer patients. Effect on salivary and serum electrolytes. *Cancer* 1976;38:273–278.
7. Karlsson G. The relative change in saliva secretion in relation to the exposed area of the salivary glands after radiotherapy of head and neck region. *Swed Dent J* 1987;11:189–194.
8. Bertram U. Xerostomia. Clinical aspects, pathology and pathogenesis. *Acta Odontol Scand* 1967;25(Suppl 49):1– 126.
9. Johnson JT, Ferretti GA, Nethery WJ, et.al. Oral pilocarpine for post-irradiation xerostomia in patients with head and neck cancer. *The New Wngland Journal of Medicine* 1993;329:390-5.
10. Rode M, Smid L, Budihna M, et.al. The influence of pilocarpine and biperiden on pH value and calcium, phosphate and bicarbonate concentrations in saliva during and after radiotherapy for head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; 92:509-14.
11. Gornitsky M, Tsang CSP, Shenouda G, Sultanem K, et.al. Double-blind randomized, placebo-controlled study of pilocarpine to salvage salivary gland function during radiotheraphy of patients with head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 98:45-52.
12. Denshen, W. A brief explanation of international standard nomenclature of zhenjiu (acupuncture & moxibustion) points. WHO. 1992: 133-203.

13. Wada A, Uchida N, Yokokawa M, Yoshizako T, Kitagaki H. Radiation-induced xerostomia: objective evaluation of salivary gland injury using MR sialography. *Am J Neuroradiol* 2009; 1-8.
14. Scarpace SL, Brodzik FA, Mehdi S, Belgam R. Treatment of head and neck cancers: Issues for clinical pharmacists. *Pharmacotherapy* 2009; 29:578-92.
15. Morganstein WM. Auricular acupuncture in the treatment of xerostomia. *Journal of Chinese Medicine* 2005; 79:5-8.
16. M, Dawidson I, Fernberg JO, Johnson G, Angmar-Manson B. Acupuncture treatment of patients with radiation-induced xerostomia. *Oral Oncol Eur J Cancer* 1996; 32B:182-90.
17. Johnstone PAS, Niemtzow RC, Riffenburgh RH. Acupuncture for xerostomia: clinical update. *Cancer* 2002; 94:1151-6.
18. Thomson WM, Williams SM. Further testing of the xerostomia inventory. *Oral Surg Oral Med Pathol Oral Radiol Endol* 2000; 89:46-50.
19. Kiswojo, Widya DK, Srilestari A. Akupunktur Medik dan perkembangannya. Kolegium Akupunktur Indonesia, Jakarta, 2009.
20. Bardow A, Pedersen AML, Nauntofte B. saliva. In: Miles TS, Nauntofte B, Svensson P (eds): Clinical oral physiology. Copenhagen: Quintessence Publishing Co Ltd. 2004, p.17-51.
21. Susworo R. Radioterapi pada berbagai kasus. Dalam: Radioterapi. Jakarta: Penerbit Universitas Indonesia 2006;64-72.
22. Emami B, Lyman J, Brown A, et al. Tolerance of normal tissue to therapeutic irradiation. *Int J Radiat Oncol Biol Phys* 1991;21:109–122.
23. Garcia MK, Chiang JS, Cohen L, et.al. Acupuncture for radiation-induced xerostomia in patients with cancer: a pilot studi. *Head Neck* 2009; 31:1360-8.

Sacral Tumor: Experience in a Single Institution

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ABSTRACT

Introduction. *Sacral tumors are rare, and experience of these tumors is usually limited to a small number of patients. In this study, we evaluated profile, survival rates, and functional outcome in a series of sacral tumor treated in our institution.*

Method. *We retrospectively reviewed the records of 22 sacral tumor patients from January 1995 to February 2014 in Cipto Mangunkusumo National Central Hospital, Jakarta, Indonesia. Kaplan-Meier method was used to described survival and functional outcome. Their correlation with clinical profile, histological type, level of sacral involvement, treatment, and complication were analyzed by Log rank test.*

Results. *From 22 patients, 5 of them were excluded from this study. Thus, there were 17 cases of sacral tumor, 16 of them were malignant and one case was benign. In Kaplan-Meier Analysis, there were no significant difference in survival found between sex, age group, biopsy type, level of sacral involvement, treatment, and complication. There was significant difference in survival found between histopathology result (p=0.012), and giant cell tumor GCT showed the highest survival, followed by chordoma, metastatic lession, and Ewing Sarcoma. Sacral tumor at the level of S2 and below had better functional outcome compared to the one above S2 (p=0.001). There were no difference in functional outcome found between histopathology type and treatment (p=0.137 and p=0.210).*

Conclusion. *The majority of primary tumors of sacrum are chordoma which present with nonspecific early signs and symptoms. Survival rate and functional outcome of the sacral tumor patients were determined by histopathology result and level of sacral involvement. Lower level of sacral involvement lead to better survival and functional outcome.*

Keyword: *sacral tumors, chordoma, giant-cell tumor, metastasis, survival, functional outcome*

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ABSTRAK

Pendahuluan. Tumor sakrum sangat jarang ditemukan; dan pengalaman mengenai tumor sakrum biasanya terbatas pada sejumlah kecil pasien. Dalam studi ini, kami mengevaluasi profil, tingkat kesintasan, dan luaran fungsional dari serangkaian tumor sakrum yang dirawat di institusi kami.

Metode. Kami telah mengevaluasi 22 pasien tumor sakrum dari Januari 1995 sampai Februari 2014 secara retrospektif di Rumah Sakit Umum Pusat Nasional Cipto Mangunkusumo Jakarta Indonesia. Metode Kaplan-Meier digunakan untuk menganalisis angka kesintasan dan luaran fungsional. Hubungan antara kesintasan dan luaran fungsional dengan profil klinis, jenis histopatologi, level sakrum yang terlibat, penatalaksanaan, dan komplikasi dianalisis dengan Log rank test.

Hasil. Dari 22 pasien, hanya 17 pasien tumor sakrum yang dimasukkan ke dalam studi ini (5 kasus diekslusi), 16 kasus dengan tumor ganas dan 1 kasus dengan tumor jinak. Hasil analisis Kaplan-Meier menunjukkan tidak ada perbedaan yang bermakna pada angka kesintasan terhadap jenis kelamin, kelompok umur, jenis biopsi, level sakrum yang terlibat, penatalaksanaan, dan komplikasi. Hasil uji statistik menunjukkan perbedaan yang bermakna antara kesintasan dengan hasil histopatologi (p = 0,012), giant cell tumor menunjukkan kesintasan hidup tertinggi, diikuti oleh Chordoma, lesi metastasis, dan Ewing Sarcoma. Tumor sakrum setinggi S2 ke bawah memiliki luaran fungsional yang lebih baik dibandingkan dengan level di atas S2 (p = 0,001). Hasil uji statistik menunjukkan tidak ada perbedaan yang bermakna

antara luaran fungsional dengan jenis histopatologi dan penatalaksanaan (p = 0,137 dan p = 0,210).

Kesimpulan. Mayoritas tumor primer pada tulang sakrum adalah chordoma yang muncul dengan gejala dan tanda-tanda awal yang tidak spesifik. Angka kesintasan dan luaran funsional pasien tumor sakrum dipengaruhi oleh jenis histopatologi dan level sacrum yang terlibat. Semakin rendah level sacrum yang terlibat, semakin baik kesintasan dan luaran fungsional.

Kata Kunci: Tumor sakrum, Chordoma, giant cell tumor, metastasis, kesintasan, luaran fungsional

INTRODUCTION

Tumors of the sacrum are rare. Its incidence among all bone tumors varies between 1% and 4.3%.[1,2] The majority of these tumors are benign aggressive lesions like giant cell tumor (GCT), aneurysmal bone cyst, osteoblastoma, and low-grade malignancies like chordoma and chondrosarcoma. These tumors usually present late on their course and may reach huge size.[1-5] Complexity of sacral neuroanatomy and its proximity to vital organs makes the management of these tumors difficult.[1,6-8] Some times, resection of the tumor may cause lumbopelvic instability and injury to important structures around the pelvis.[1-2,5]

Clinical outcomes of sacral tumor depend on several factors such as type of the tumor (histopathology), size of the tumor, neurological symptoms, and treatment approach.[1,4,6,8] Intralesional resection with chemocauterization or thermocauterization may be a curative treatment for benign lesions. On the other hand, wide resection combined with chemotherapy and radiotherapy is necessary in malignancies.[1,2,5-8]

Until recently, only few studies have described about therapeutic outcome of sacral tumor. In this study, we reviewed clinical outcomes and survival rate in a series of patients treated for sacral tumor in our institution.

MATERIAL AND METHODS

We retrospectively reviewed the records of 22 sacral tumor patients treated in Cipto Mangunkusumo National Central Hospital of Indonesia from January 1995 to February 2014. Five patients were excluded from this study due to three patients refused to receive therapy, one patient diagnosed as rhabdomyosarcoma (soft tissue tumor) and one patient diagnosed as tuberculosis (chronic infection). Therefore, we evaluated seventeen sacral tumor subjects only.

Presenting symptom was complain that encourage patients to seek treatment. In this study the presenting symptoms were pain and mass in sacral area. Biopsy types were classified into fine needle aspiration (FNA), core needle, and open biopsy. Final diagnosis of every cases was established by clinical, radiological (plain radiographs, computed tomography, or magnetic resonance imaging scan), and histopathological findings in clinicopathological conference (CPC). Diagnosis of the tumors was divided into malignant (chordoma, Ewing sarcoma, and metastatic bone disease) and benign tumor (GCT) groups. We classified functional status into; dependent (crutch, wheelchair, and bed) and independent groups. Postoperatively, we evaluated patient's functional status, complication, and survival rate. Variables collected were; ages, gender, presenting symptom, duration of symptom, type of biopsy, histopathological type, level of sacral involvement (above S2, S2 and below), type of surgical and non-surgical management, complications, and survival rate. Data were retrieved from orthopaedic oncology registry records (table 1).

Table 1: Demographic and clinical information of the patients

No	Sex/ Age	Symptom	Duration OOf Symptom	Type of Biopsy	Diagnosis	Level	Treatment	Complication after therapy	Survival	Duration of Follow up	Ambulatory status
1	M/38	Pain	4 mo	Open biopsy	Chordoma	S1-S3	Radiotherapy	Pain with weightbearing (WB)	7 years	7 years	Crutch (dependent)
2	M/48	Pain	`n/a	Open biopsy	Chordoma	S1-S5	Sacrectomy	Post op: saddle hypesthesia + sphincter ani weakness (motoric + sensoric)	1 year	1 year	Wheelchair (dependent)

No	Sex/ Age	Symptom	Duration OOf Symptom	Type of Biopsy	Diagnosis	Level	Treatment	Complication after therapy	Survival	Duration of Follow up	Ambulatory status
4	M/47	Pain	2 yr	Open biopsy	Chordoma	S4-S5	Chemotherapy	None	8 month	8 months	Walk Independent
5	M/41	mass	1 yr	Open biopsy	Chordoma	S1-S5	Radiotherapy	Pain with WB	Alive	108 months	Crutch (dependent)
6	F/35	pain	3 months	Open biopsy	Giant cell tumor	S1-S3	Radiotherapy	Motoric + sensoric	Alive	96 months	Wheelchair (dependent)
7	F/55	pain	8 months	FNAB	Chordoma	S1-S4	Chemotherapy	Saddle anesthesia (sensoric)	Died 7 years	7 yrs	Crutch (dependent)
8	F/22	Pain + Motor deficit	10 months	Open biopsy	Metastasis Neuroblastoma	S1-S2	Chemotherapy	None	1 year	1 year	Bedridden (due to general condition)
9	F/22	pain	6 months	Open biopsy	Ewing sarcoma	S1-S4	Radiotherapy	Respiratory failure + sepsis	2 months	2 months	Bedridden (dependent)
10	M/59	Pain	6 months	Open biopsy	Chordoma	S1-S5	Sacrectomy	Sepsis	1 day post op	1 day	Bedridden (dependent)
11	F/47	pain	3 months	Core biopsy	Chordoma	S1-S5	Sacrectomy	Motor deficit	Alive	24 months	Crutch (dependent)
12	F/47	pain	6 months	Core biopsy	Metastasis Ca. cervix	L4-S2	Radiotherapy	Motor deficit	1 year	1 year	Wheelchair Walk independent
13	F/37	pain + mass	8 months	Core biopsy	Osteosarcoma + bone metastasis regio sacrum + pelvis	L5-S2	None	Respiratory failure + sepsis	1 month	1 month	Bedridden Walk independent
14	F/57	pain	6 years	Open biopsy	Chordoma	S2-S5	Sacrectomy + radiotherapy	Pain with WB	Alive	22 months	Walk independent
15	M/27	Pain	3 months	Core biopsy	Chordoma	S4-S5	Sacrectomy	None	Alive	20 months	Walk independent
16	M/61	Pain	4 months	Core biopsy	Chordoma	S1-S5	Chemotherapy	n/a	2 years	2 years	Wheelchair (dependent)
17	F/57	Pain	3 years	Core biopsy	Chordoma	S3-S5	Sacrectomy	None	Alive	5 months	Wheelchair (dependent)

F : female
M : Male
LOF : Loss of follow up
RT: Refused any treatment
+ : death after

Kaplan-Meier method was used to described survival and functional outcome. Their correlation with clinical profile, histological type, level of sacral involvement, treatment, and complication were analyzed by Log rank test. The correlation between histopathology types, groups of sacral involvement and treatment group to functional status was analyzed by chi square test.

RESULTS

From 17 patients, there were 8 males and 9 females with a median age 47 years old (range 22 to 61 years). The most common symptom was pain. Only two patient came with complain of mass and no patient who had only neurologic deficit. The median duration of symptom before diagnosis was 8 months (range 3 months to 6 years). Twelve patients presented with chordoma, one patient with Ewing sarcoma, three cases of metastasis, and one patient presented with giant cell tumor (GCT). Most of the biopsy types (ten cases) were open biopsy, six cases with core biopsy, and one FNAB. Six patients were treated with radiotherapy only, six patients with surgical excision, four patient with chemotherapy only, one patient with radiotherapy, surgical excision, and embolization. Most of the patients did not have any complication after surgical sacrectomy. There were 2 patients who complain incontinence and two others complain saddle hypesthesia and motoric weakness. One patient died due to postoperative thrombosis and sepsis. These data were summarized in table 1.

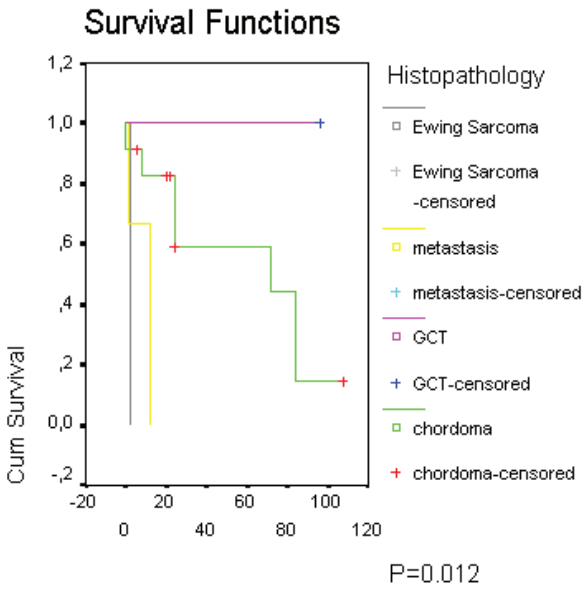

Figure 1: Kaplan-Meier Analysis of Survival Difference between Histopathology group. There was significant difference in survival (p=0.012).

The median survival was 24 months, five year survival rate were 29%. In Kaplan-Meier Analysis, there were no significant difference in survival found between sex, age group, biopsy type, treatment, and complication. There was significant difference in survival found between histopathology result (p=0.012), GCT showed the highest survival, followed by chordoma, metastatic lession, and Ewing Sarcoma (figure 1). Sacral tumor at the level of S2 and below had better functional outcome (walk independently) compared to the one above S2 (p=0.001). There were no difference in functional outcome found between histopathology types and treatment group (p=0.137 and p=0.210).

DISCUSSION

Primary sacral tumors are rare lesions that account between 1% to 4.3% and fewer than 7% of all intraspinal primary tumors.[9-10] Metastatic lesions, multiple myeloma, and lymphoma are far more common than primary sacral tumors.[11-12] However in our series, primary sacral tumors are more common than metastatic lesions or multiple myeloma. That difference may occur because not all patients with metastatic lesions or multiple myeloma came to orthopaedic care. Hence it is not necessarily represent actual condition. As mentioned in the literature, the most common case of primary tumor of the sacrum was chordoma, this finding is similar with our series.[13]

Patients with sacral tumor present with nonspecific symptoms such as; pain, palpable mass, and neurologic deficits.[12] In this study, the most common presenting symptom was pain in the sacral region. Only two patients presented with mass. Meanwhile, no patients with sacral tumor in our study came with neurologic deficit as the presenting symptom. In chordoma, sacral GCTs, and metatastic lesions the initial manifestation usually local pain over the sacrum or lumbosacral junction that frequently radiate into the posterior aspect of one or both thighs. Pain in sacral tumor was thought to be caused by the mass effect and also impingement of surrounding structures. The onset of pain is determined from the growing nidus where the evolution of symptom follows the growth pattern of tumor.[13]

While pain was the most common presenting symptom, mean duration of symptom of sacral tumor was different between histopathological type. Pain in bone tumor was also determined by its progressivity. Sacral chordomas are slow-growing, gelatinous, extradural tumors with areas of hemorrhage and necrosis that often reach a large

size and cause late-onset compressive neurological symptoms. Thus, in chordoma, pain might present for a long time before a mass is palpable or lytic lession is demonstrable by x-ray.[14]). In our study, the median duration of symptoms prior to diagnosis in sacral chordoma is 10 months. However, GCT and metastatic lesions were more aggresive than chordomas, so their symptom manifest more early. In other words, GCT and metastatic lession had shorter duration of symptom than chordoma.[15]

Biopsy was the final step in diagnostic process of sacral tumor and should not be performed unless all noninvasive studies have been completed. [16] Decision making in these lesions depended on a variety of factors. Some authors recommended open biopsy for diagnosis, but others were satisfied with the adequacy of material and accuracy of diagnosis obtained with CT-guided core needle biopsy (CNB) (17-18). Before 2011, almost all of our diagnostic procedures were open biopsy, after that we performed CNB with or without CT guide. The later procedure had the advantage of reducing local contamination, ensuring excision of the biopsy tract at the time of definitive surgery, less invasive, and may be done with local anesthesia. In addition, we have conducted immunohistochemistry staining from the representative specimen obtained by CNB.

Preoperative embolization was said to be effective in decreasing the amount of blood loss, but in our case there was one patient who underwent preoperative embolization died due to thrombosis of femoral artery and sepsis. In several studies, the use of preoperative embolization was criticized.[8,19]

Main goal in the management of sacral tumors are maximizing disease control and minimizing neurological disfunction.[1] Several studies has showed improvement in functional outcome and survival rate associated with the surgical procedure.[8,20-22] In our series, 32% of the patients had neurological deficit (motoric and sensoric). The desire to protect the nerve and inability to use adjuvant may influence adequacy of tumor resection. On the other hand, aggressive surgery may result in neurological disfunction. The extent of lesion determine the approach while planning for wide excision in sacral tumors. Those lesions that have the upper extent above S4 are best excised with a combined anterior and posterior approach while those at or below S4

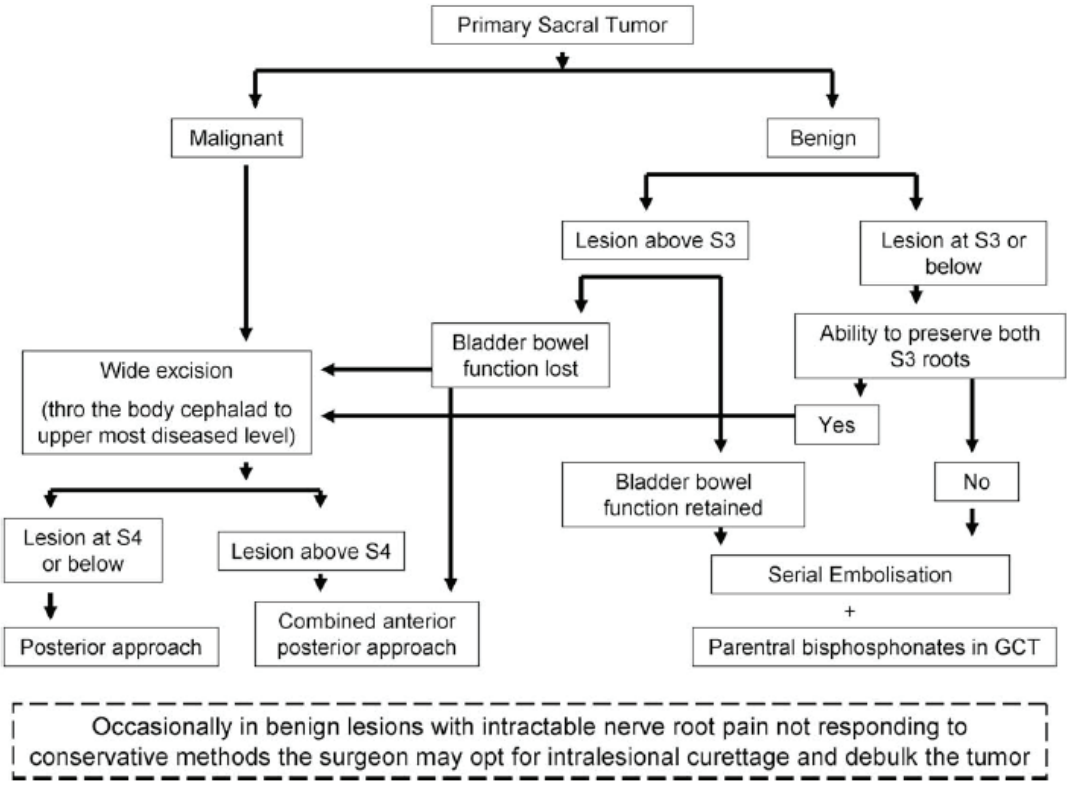

Figure 2: Strategy in Management of Sacral Tumor (1).

can be adequately excised with a posterior approach only. If the surgeon is able to reach above the mass on rectal examination then a posterior approach alone is sufficient for excision.[1]

Curretage in large and expanded lesion which extend above S3 is often difficult because of difficult exposure and massive blood loss. In a review by Cheng et al., no disfunction in defecation and urination were found if the S3 root was preserved.[15] Todd et al. said that in patient who undergone sacral resection with preservation of bilateral S3 root, the function of urination and defecation is preserved (100% and 69% respectively), therefore it is recommended that all the S3 root should be preserved in patients who will be treated by wide resection (Figure 2).[23] More cephalad levels of resection (cephalad to S2) were associated with poorer bladder control.[8] In our series, most of the patient with sacral involvement above S2 had neurological deficit. This correlates with the extent of the lesion and preservation of the nerve root. There appears to be some variability in clinically observed neurophysiologic control.

Chemotherapy is another modality in treatment of chordoma. The effectiveness of chemotherapy has been largely been reported using anecdotal responses to anthracyclines, cisplatin, and alkylating agents, as well as targeted therapies such as cetuximab, gefitinib, thalidomide, and erlotinib.[24-27] Chordoma overexpresses platelet-derived growth factor receptor (PDGFR)-β and its phosphorylated form, denoting constitutive activation.[28] Subjective pain relief was reported in 64% symptomatic patients. Other molecularly target agents (cetuximab, gefitinib) and antiangiogenic therapy with thalidomide were tested in single cases of chordomas with interesting results.[29-30] In our series, there were 2 patient who have been treated by chemotherapy because they refused surgical procedure but the treatment regiment was unclear due to lack of information in medical record. One of the consideration of using the chemotheurapeutic agent is in advanced disease extension and progression. This was shown in our series that 2 patient died in less than 2 years indicating that the disease was already advanced.[31-32]

Kaplan-Meier test showed that there was no significant difference in survival between benign and malignant lesions and also no significant difference between treatments, this may be due to patients with either malignant or benign lesions (especially GCT), usually came to our hospital in an already advanced stage where the lesion was too large and involving neurovascular structure. This condition makes the surgery, radiotherapy, and chemotherapy only available for palliative means. Nevertheless, there was significant difference in survival found between histopathology result, GCT showed the highest survival, followed by chordoma, metastatic lession, and Ewing Sarcoma.

Functional outcome of patient with sacral tumor depends on the presence of neurologic deficit, which basically determined the patient's quality of life. Defecation and urination still normal if the bilateral S3 root or unilateral S1-S5 root is intact.[24] Functional outcome in this study was limited on neurological complication and ambulatory status of the patients. Statistical analysis showed no significant difference between functional status and histopathology types or treatment group. This result might be caused by the late presentation of patients and thus, complete surgical excision could not be performed. Patient with lession above S2 had lower functional outcome compared to the one who had lession at the level of S2 and below, this difference was statistically significant ($p=0.001$). Meanwhile, three of four patient who had the lession at S2 and below could walk independently. Symptom of weakness on lower extremity was elicited when S1 root was sacrificed. Meanwhile, patients with intact L5 root could walk without assistive devices.[24] A multicenter study with larger number of subject was needed to determine the exact relationship between patient profile, radiological and histological characteristic, level of sacral involvement, and survival as well as functional result.

CONCLUSION

The majority of sacral tumors are chordomas which are low-grade malignancy with unspecific signs and symptoms. The approach in sacral tumor needs multidiciplinary team to obtain adequate diagnosis and management. A good management of the patients especially wide resection with adequate margin for chordoma may give good local control and clinical outcome. Survival rate and functional outcome of the sacral tumor patients were determined by histopathology result and level of sacral involvement. Earlier diagnosis and lower level of sacral involvement lead to better survival and functional outcome.

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REFERENCES

1. Puri A, Agarwal MG, Shah M, Srinivas CH, Shukla PJ, Shrikhande SV, Jambhekar NA. Decision making in primary sacral tumors. *Spine J* 2009;9(5):396-403.
2. Sar C, Eralp L. Surgical treatment of primary tumors of the sacrum. *Arch Orthop Trauma Surg* 2002;122(3):148-55.
3. Samson IR, Springfield DS, Suit HD, Mankin HJ. Operative treatment of sacrococcygeal chordoma, a review of twenty-one cases. *J Bone Joint Surg Am* 1993;75(10):1476-84.
4. Simpson AH, Porter A, Davis A, Griffin A, McLeod RS, Bell RS. Cephalad sacral resection with a combined extended ilioinguinal and posterior approach. *J Bone Joint Surg Am* 1995;77(3):405-11.
5. Sung HW, Shu WP, Wang HM, Yuai SY, Tsai YB. Surgical treatment of primary tumors of the sacrum. *Clin Orthop Relat Res* 1987;215:91-8.
6. Wuisman P, Lieshout O, Sugihara S, vanDijk M. Total sacrectomy and reconstruction: oncologic and functional outcome. *Clin Orthop Relat Res* 2000;381:192-203.
7. Wuisman P, Lieshout O, vanDijk M, vanDiest P. Reconstruction after total en bloc sacrectomy for osteosarcoma using a custom-made prosthesis: a technical note. *Spine* 2001;26(4):431-9.
8. Hulen CA, Temple HT, Fox WP, Sama AA, Green BA, Eismont FJ. Oncologic and functional outcome following sacrectomy for sacral chordoma. *J Bone Joint Surg Am* 2006;88(7):1532-9.
9. Murphey MD, Andrews CL, Flemming DJ, Temple HT, Smith WS, Smirniotopoulos JG. Primary tumors of the spine: radiologic pathologic correlation. *Radiographics* 1996;16(5):1131-58.
10. Feldenzer JA, McGauley JL, McGillicuddy JE. Sacral and presacral tumors: problems in diagnosis and management. *Neurosurgery* 1989;25(6):884-91.
11. Gibbs IC, Chang SD. Radiosurgery and radiotherapy for sacral tumors. *Neurosurg Focus* 2003;15(2):E8.
12. Llauger J, Palmer J, Amores S, Bague S, Camins A. Primary tumors of the sacrum: diagnostic imaging. *Am J Roentgenol* 2000;174(2):417-24.
13. Payer M. Neurological manifestation of sacral tumors. *Neurosurg Focus* 2003;15(2):E1.
14. Mabrey RE. Chordoma: a study of 150 cases. *Am J Cancer* 1935;25:501-17.
15. Cheng EY, Ozerdemoglu RA, Transfeldt EE, Thompson RC Jr. Lumbosacral chordoma: prognostic factors and treatment. *Spine* 1999;24(16):1639-45.
16. Leithner A, Maurer-Ertl W, Windhager R. Biopsy of bone and soft tissue tumors: hints and hazards. In: Tunn PU, editor. Treatment of bone and soft tissue sarcomas. 2009. Berlin: Springer-Verlag.p3-9.
17. Ozerdemoglu RA, Thompson RC Jr, Transfeldt EE, Cheng EY. Diagnostic value of open and needle biopsies in tumors of the sacrum. *Spine* 2003;28(9):909-15.
18. Puri A, Shingade VU, Agarwal MG, Anchan C, Juvekar S, Desai S, Jambhekar NA. CT-guided percutaneous core needle biopsy in deep seated musculoskeletal lesions: a prospective study of 128 cases. *Skeletal Radiol* 2006;35(3):138-43.
19. Papagelopoulos PJ, Choudhury SN, Frassica FJ, Bond JR, Unni KK, Sim FH. Treatment of aneurysmal bone cysts of the pelvis and sacrum. *J Bone Joint Surg Am* 2001;83-A(11):1674-81.
20. Yang H, Zhu L, Ebraheim NA, Liu J, Shapiro A, Castillo S, Liu X, Tang T. Surgical treatment of sacral chordomas combined with transcatheter arterial embolization. *J Spinal Disord Tech* 2010;23(1):47-52.
21. Li D, Guo W, Tang X, Ji T, Zhang Y. Surgical classification of different types of en bloc resection for primary malignant sacral tumors. *Eur Spine J* 2011;20(12):2275-81.
22. Ozger H, Eralp L, Sungur M, Atalar AC. Surgical management of sacral chordoma. *Acta Orthop Belg* 2010;76(2):243-53.
23. Todd LT Jr, Yaszemski MJ, Currier BL, Fuchs B, Kim CW, Sim FH. Bowel and bladder function after major sacral resection. *Clin Orthop Relat Res* 2002;397:36-9.
24. Varga PP, Bors I, Lazary A. Sacral tumors and management. *Orthop Clin North Am* 2009;40(1):105-23.
25. Walcott BP, Nahed BV, Mohyeldin A, Coumans JV, Kahle KT, Ferreira MJ. Chordoma: current concepts, management, and future directions. *Lancet Oncol* 2012;13(2):e69-76.
26. Bydon M, Papadimitriou K, Witham T, Wolinsky JP, Bydon A, Sciubba D, Gokaslan Z. Novel therapeutic targets in chordoma. *Expert Opin Ther Targets* 2012;16(11):1139-43.
27. Stacchiotti S, Longhi A, Ferraresi V, Grignani G, Comandone A, Stupp R, Bertuzzi A, Tamborini E, Pilotti S, Messina A, Spreafico C, Gronchi A, Amore P, Vinaccia V, Casali PG. Phase II study of imatinib in advanced chordoma. *J Clin Oncol* 2012;30(9):914-20.
28. Tamborini E, Miselli F, Negri T, Lagonigro MS, Staurengo S, Dagrada GP, Stacchiotti S, Pastore E, Gronchi A, Perrone F, Carbone A, Pierotti MA, Casali PG, Pilotti S. Molecular and biochemical analyses of platelet-derived growth factor receptor (PDGFR) B, PDGFRA, and KIT receptors in chordomas. *Clin Cancer Res* 2006;12(23):6920-8.
29. Hof H, Welzel T, Debus J. Effectiveness of cetuximab/gefitinib in the therapy of a sacral chordoma. *Onkologie* 2006, 29(12):572-4.
30. Schönegger K, Gelpi E, Prayer D, Dieckmann K, Matula C, Hassler M, Hainfellner JA, Marosi C. Recurrent and metastatic clivus chordoma: systemic palliative therapy retards disease progression. *Anticancer Drugs* 2005;16(10):1139-43.
31. Yurter A, Sciubba DM, Gokaslan ZL, Kaloostian PE. Spinal chordomas: current medical and surgical management. *JSM Neurosurg Spine* 2013:2(1):1013.
32. Ferraresi V, Nuzzo C, Zoccali C, Marandino F, Vidiri A, Salducca N, Zeuli M, Giannareli D, Cognetti F, Biagini R. Chordoma: clinical characteristics, management, and prognosis of a case series of 25 patients. *BMC Cancer* 2010;10:22.

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